

¹ Macapype: An open multi-software framework for non-human primate brain anatomical MRI processing

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DOI: [10.xxxxxx/draft](https://doi.org/10.xxxxxx/draft)

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⁹ Macapype: An Open Multi-Software Framework for Non-Human ¹⁰ Primate Brain Anatomical MRI Processing

¹¹ Summary

¹² Although brain anatomical Magnetic Resonance Imaging (MRI) processing is largely standard-
¹³ ized and functional in humans, it remains a challenge to define robust processing pipelines
¹⁴ for the segmentation of non-human primate (NHP) images. To unify the processing of NHP
¹⁵ anatomical MRI, we propose Macapype, an open-source framework to create custom pipelines
¹⁶ for data preparation, brain extraction, and brain segmentation.

¹⁷ Statement of Need

¹⁸ Non-human primates (NHPs) are increasingly used for neuroimaging studies due to the progress
¹⁹ of MR acquisitions and the promises it holds in the field of neuroscience ([Milham et al., 2018](#)).
²⁰ Structural MR images are essential for accessing anatomical information, defining regions
²¹ of interest for functional and diffusion studies, providing cortical surface reconstruction, or
²² localizing implanted electrodes for electrophysiology. Despite the standardization of MRI
²³ processing in humans with several well-known software options available, such as AFNI ([Cox, 1996](#)),
²⁴ FSL ([Smith et al., 2004](#)), SPM12 ([Frackowiak et al., 1997](#)), and ANTS ([Avants et al., 2011](#)),
²⁵ defining robust processing pipelines for NHP anatomical image segmentation remains
²⁶ difficult. Standard human pipelines do not work directly on NHP images due to differences
²⁷ in head geometry, size, and anatomical content (e.g., large muscles). Moreover, acquisition
²⁸ parameters and experimental settings are much more variable in NHP studies than in human
²⁹ studies, making it challenging to define a single method to segment properly anatomical MR
³⁰ images of all NHP species. Therefore, there is a real need for efficient, versatile software that
³¹ can handle the variability of encountered images.

³² Related Packages

³³ Several methods have been proposed to address the issue of NHP anatomical MR image
³⁴ segmentation. Some of these have been built as adaptations of existing methods originally
³⁵ developed for human images. For instance:

- ³⁶ ▪ **NHP-Freesurfer**: An adaptation of Freesurfer ([Fischl, 2012](#)) that uses the NMT macaque
³⁷ atlas to segment macaque images and extract surfaces.
- ³⁸ ▪ **CIVET-Macaque**: An adaptation of the CIVET method ([Lepage et al., 2021](#)) to extract
³⁹ cortical surfaces from macaque MR images.

- 40 ▪ **PREEMACS**: Uses various functions from FSL , ANTS , MRTrax (Tournier et al., 2019),
41 MRIqc (Esteban et al., 2017), and Freesurfer (Fischl, 2012) to extract cortical surfaces
42 from MR images and register them to the same template.
43 ▪ **Precon-all**: Uses a combination of ANTS, FSL, and Freesurfer to segment images and
44 extract surfaces. A major drawback is the dependencies on five user-defined masks,
45 including a brain mask, left and right hemisphere masks, a non-cortical mask (cerebellum
46 and brain stem), and a subcortical (medial wall) mask.
47 ▪ **U-Nets**: Used to perform brain extraction from macaque MR images (Zhong et al.,
48 2021).
49 ▪ **nBEST**: DeepLearning program used to provide brain mask, segmentation of GM, WM
50 and subcortical nuclei (Zhong et al., 2024). *Requires the use of GPUs, and performs*
51 *relatively badly on small PNH species such as marmoset.*
- 52 Unfortunately, none of these software solutions are versatile and flexible enough to fully perform
53 segmentation while handling the variety of species and image characteristics encountered in
54 NHP neuroimaging studies.

55 Presentation of the Package

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

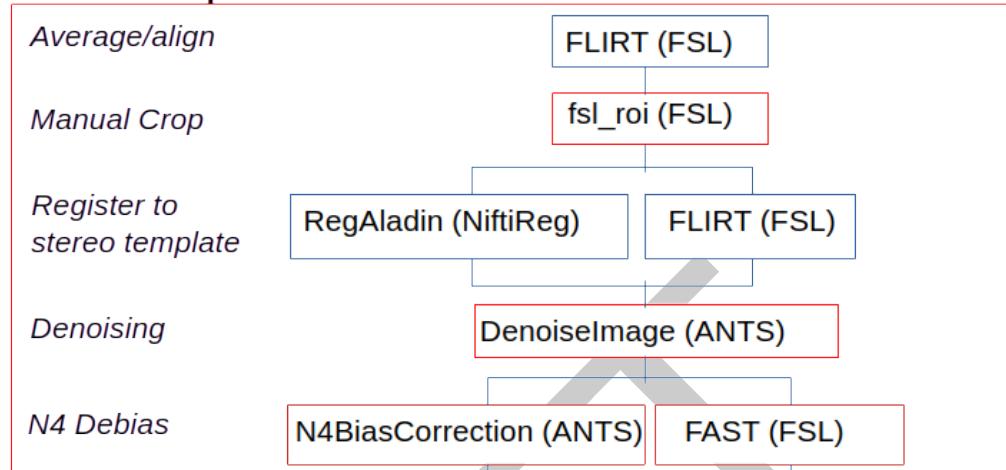
63 The Macapype package was specifically designed to provide:

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

71 Pipelines

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

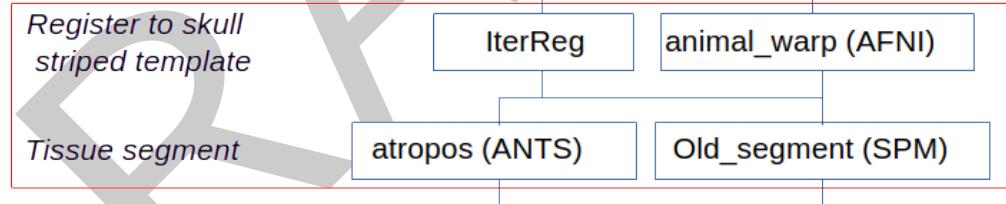
Data Preparation



Brain Extraction



Brain Segmentation



Post processing

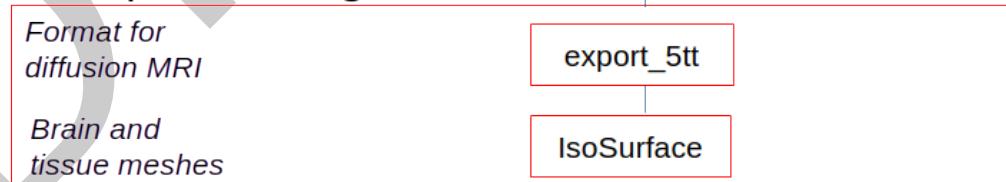


Figure 1: Different pipelines are chained

⁷⁶ Data Preparation Pipeline

⁷⁷ The composition and order of the steps in the data preparation pipeline are specified in a json
⁷⁸ parameters 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 `fslreorient2std` 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).

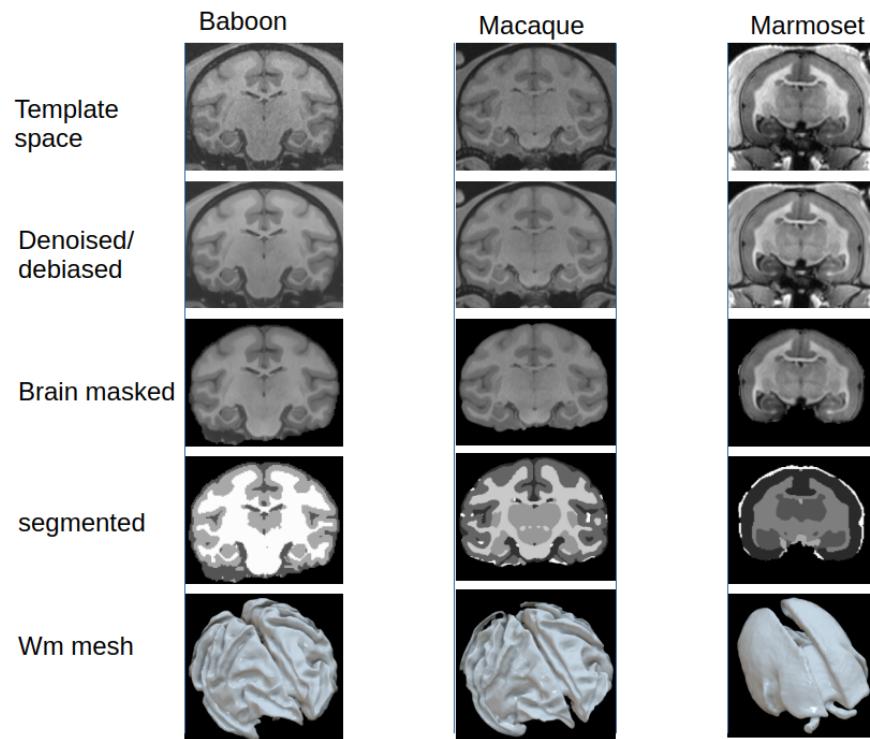


Figure 2: Different species at different steps of the processing

116 Discussion

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

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

132 Acknowledgements

133 We are grateful to Adrien Meguerditchian, Paul Apicella and Guilhem Ibos for using sample of
 134 their MRI datasets as examples and tests on the different species.

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