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# A Unified, End-to-End Pipeline Solution for Human and Nonhuman Functional Connectomics

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## Introduction

Macroscale neuroimaging techniques in human and nonhuman animal models are critical to the development of a multilevel understanding of human brain function. However, the necessary tools for organizing, processing and analyzing neuroimaging data generated through these efforts are not widely available as coherent and easy-to-use software packages. Gaps are particularly apparent for nonhuman data (i.e., monkey, rodent), as most of the existing processing and analytic software packages are specifically designed for human imaging.

Methods have been proposed for addressing the challenges inherent to the processing of nonhuman data (e.g., brain extraction, tissue segmentation, spatial normalization, brain parcellation, temporal denoising); to date, these have not been readily integrated into an easy-to-use, robust, and reproducible analysis package. As a result, translational and comparative neuroimaging researchers patch together neuroinformatics pipelines that use various combinations of disparate software packages and in-house code. Here we report on recent efforts to extend the Configurable Pipeline for the Analysis of Connectomes (C-PAC) open-source software to handle animal imaging data, thereby providing a unified platform for the robust and reproducible analysis of human and nonhuman MRI data.

## Methods

Two nonhuman pipelines were identified, one for the macaque monkey based on the work of Xu et al. (2019) and the other for the rodent based on the work of Pagani et al. (2019). Specific methods added to facilitate NHP processing include:

1) U-Net based skull extraction;
2) non-local means spatial-filter denoising;
3)ANTs-prior based tissue segmentation. Specific methods added to facilitate rodent data processing include:
1) scaling;
2) template based tissue segmentation;
3)EPI-based image registration.

General methods added to improve processing include N4 bias correction for anatomical and functional image. Spatial correlation between key intermediates (e.g., anatomical in template space) was used to evaluate registration and segmentation performance, as these are common bottlenecks for processing NHP data. Independent component analysis (ICA) and seed based correlation analysis (SCA) was employed to generate sample outputs for comparison between pipelines.

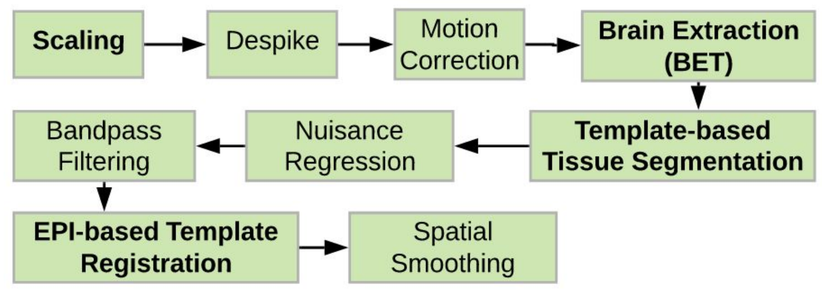



Figure 1. Key steps of rodent preprocessing

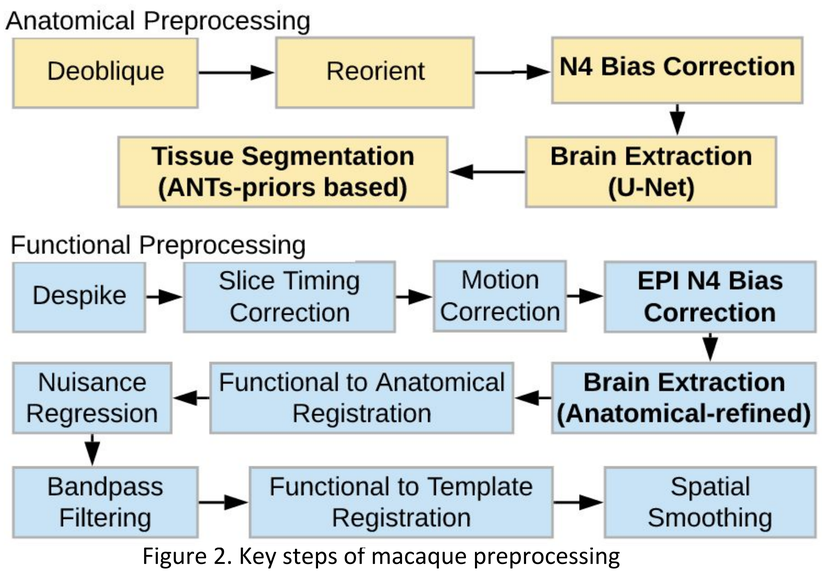
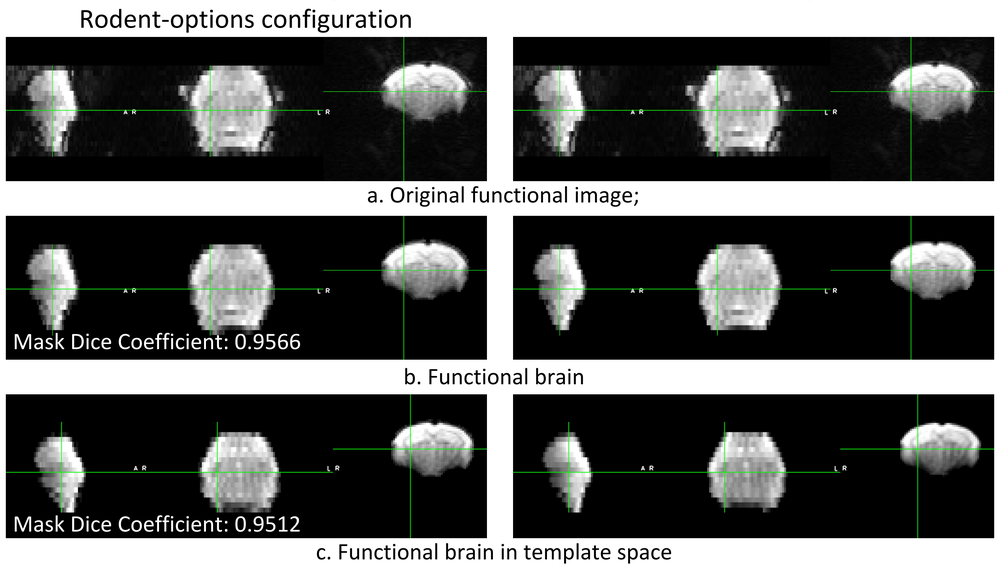



Figure 2. Key steps of macaque preprocessing

## Results




a. Original functional image;
b. Functional brain
c. Functional brain in template space

Figure 3. Rodent functional preprocessing visual comparison.

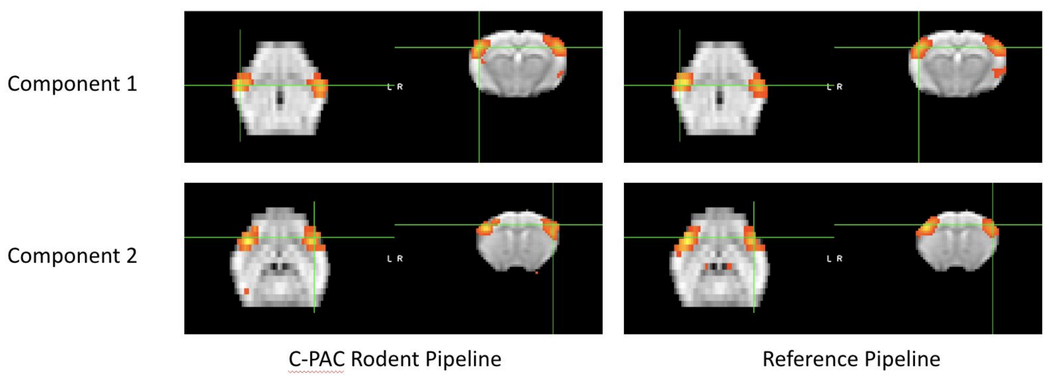



Figure 4. Correspondence between C-PAC Rodent Pipeline and Reference Pipeline

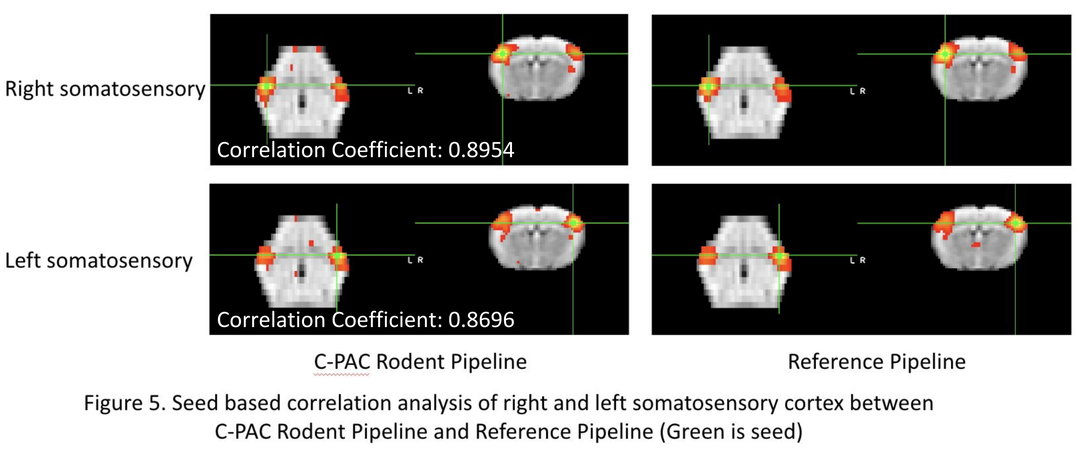
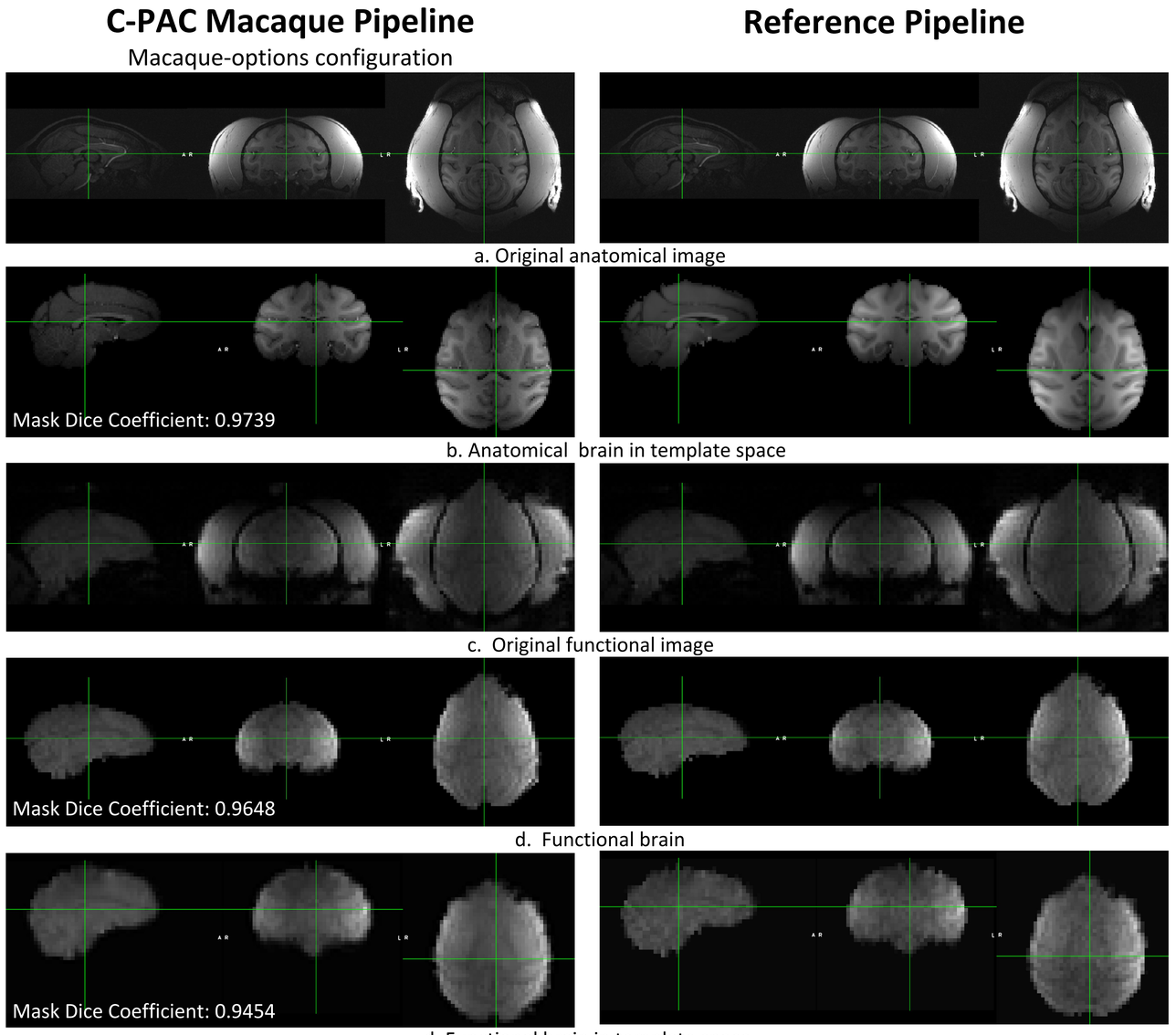



Figure 5. Seed based correlation analysis of right and left somatosensory cortex between C-PAC Rodent Pipeline and Reference Pipeline (Green is seed)




a. Original anatomical image
b. Anatomical brain in template space
c. Original functional image
d. Functional brain
d. Functional brain in template space

Figure 6. Macaque preprocessing visual comparison

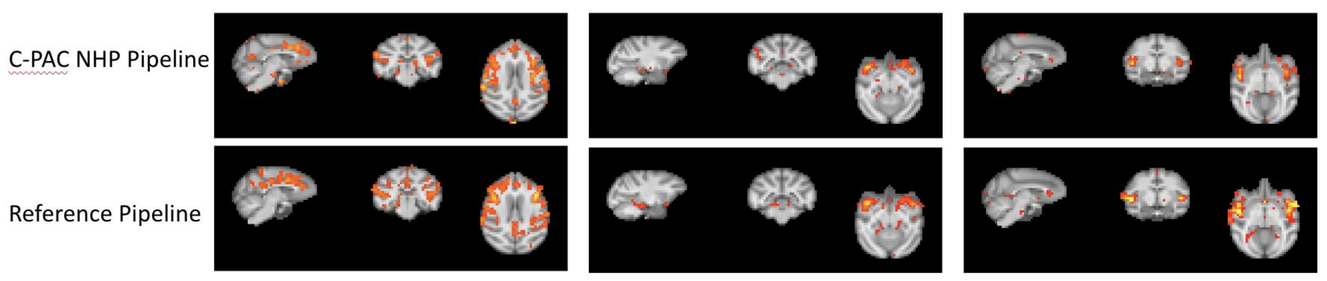



Figure 7. Correspondence between C-PAC NHP Pipeline and Reference Pipeline

Implementation of the proposed changes through an iterative release cycle enabled the human-focused C-PAC pipeline to successfully process full-brain nonhuman primate and rodent data (i.e, mouse). Examples of key step outputs and the correspondence (from ICA) to those from reference pipelines are depicted in Figures 3 and 4 for rodent, and Figure 6 and 7 for macaque. Figure 5 shows seed based correlation analysis-based functional connectivity maps for the rodent data. Importantly, the analytic pipeline using the nonhuman configurations were able to run in an entirely automated fashion, which is essential for C-PAC to become a scalable, end-to-end tool for nonhuman and human analysis.

## Conclusions

Initial results demonstrate the feasibility of achieving high correspondence between the results generated using reference nonhuman pipelines (i.e., rodent, nonhuman primate) and those obtained using the nonhuman pipeline configurations in C-PAC. Our next step will be the scaling of testing to include the entirety of datasets included in the PRIMatE Data Exchange (PRIME-DE). The configurations employed in the present work, and the functionality employed, are made available in the C-PAC v1.6.2 release (http://fcp-indi.github.io).

## Reference

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[3] Russ, Brian E., et al. "Distinct fMRI responses to self-induced versus stimulus motion during free viewing in the macaque." Journal of Neuroscience 36.37 (2016): 9580-9589.
[4] Sharad, S. et al. (2014). Towards Automated Analysis of Connectomes: The Configurable Pipeline for the Analysis of Connectomes (C-PAC). Frontiers in Neuroinformatics, 8. doi: 10.3389/conf.fninf.2014.08.00117