

# PhiPipe Manual (v1.2.0)

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## 1. Background

PhiPipe is a processing pipeline for multi-modal MRI brain images, which was developed at [Psychological Health and Imaging Group](#).

## 2. Dependent softwares

Required:

[FreeSurfer](#) 6.0.0

[FSL](#) 5.0.11/6.0.0/6.0.2

[AFNI](#) 17.2.07/18.3.03/20.0.19

[ANTs](#) 2.2.0

[Convert3D](#) 1.0.0

[R](#) 3.5.2/3.6.1

[oro.nifti](#) 0.9.0/0.10.3/0.11.0

[ImageMagick](#) 6.7.2-7

Optional:

[MATLAB](#) R2015b

[SPM12](#) 7219

[CAT12](#) 1434

The software versions listed above were tested and other versions might (not) work. Execute the script *check\_dependencies.sh* to check whether the required softwares have been successfully installed or configured.

## 3. How to use PhiPipe?

(1) Set the environmental variable to make PhiPipe scripts globally accessible, for instance,  
*export PhiPipe=/home/alex/code/PhiPipe*

(2) The three scripts, namely, *t1\_process.sh*, *bold\_process.sh* and *dwi\_process.sh*, are used to process T1-weighted/BOLD fMRI/Diffusion-weighted images (DWI) in a pipeline manner; T1 image is a must for processing BOLD and DWI images; Execute these scripts without any options to see example usages.

(3) An example script *example\_script.sh* in the *examples* folder illustrates the typical usage, and a few parameters should be modified to match the data at hand.

(4) For BOLD, repetition time (TR) and slice timing information should be provided; For DWI, b-

value/b-vector files, and phase encoding direction should be provided; These information could be obtained from the JSON file if dicom-to-nifti conversion is performed using [dcm2niix](#).

(5) Absolute path should be used whenever a path is needed.

#### **4. The general processing steps**

For T1:

(1) Use FreeSurfer's *recon-all* to perform skull stripping, tissue segmentation, surface reconstruction, anatomical parcellation, etc. Optionally, the skull stripping could be done using CAT12 instead of FreeSurfer.

(2) Parcellate the cortical surface using Schaefer Atlas.

(3) Create masks and quality control pictures for whole brain, gray matter, white matter, ventricle, and parcellations based on *recon-all* results.

(4) Extract cortical thickness/area/volume measures for DK Atlas and Schaefer Atlas, and subcortical volume measures for Aseg Atlas.

(5) Nonlinear registration between T1 brain image and MNI152 T1 brain template. The registration results are used in the BOLD processing.

For BOLD:

(1) Removing the first 5 volumes.

(2) Motion correction and create measures to quantify head motion.

(3) Slice timing correction.

(4) Boundary-based registration between median volume and T1 image.

(5) Create masks and quality control pictures for whole brain, gray matter, white matter, ventricle, and parcellations.

(6) Detect volumes with large head motion (motion outliers) and interpolate by neighboring volumes (i.e., motion censoring).

(7) Nuisance regression, in which mean white matter/ventricle signals and Friston's 24-parameter head motion model are included.

(8) Bandpass filtering (e.g., 0.01-0.1Hz).

- (9) Grand mean scaling to 10000.
- (10) Transform images to MNI152 standard space by combining T1-MNI152 and BOLD-T1 registration results.
- (11) Calculate functional connectivity matrix for DK+Aseg/Schaefer+Aseg Atlases.
- (12) Calculate ReHo and extract mean ReHo for DK+Aseg/Schaefer+Aseg Atlases.
- (13) Calculate ALFF/fALFF and extract mean ALFF/fALFF for DK+Aseg/Schaefer+Aseg Atlases.

For DWI:

- (1) Boundary-based registration between B0 image (the first volume) and T1 image.
- (2) Create masks and quality control pictures for whole brain and parcellations.
- (3) Eddy correction, motion correction and outlier replacement.
- (4) Diffusion tensor model fitting, calculate FA/MD/AD/RD measures and transform these measures into MNI152 space by registering FA image into the FA58\_FMRIB template.
- (5) Extract mean FA/MD/AD/RD for JHU Label/Tract Atlases.
- (6) Calculate connectivity probability matrix for DK+Aseg/Schaefer+Aseg Atlases using probabilistic tractography.

## 5. The output files

For T1:

- (1) The *t1\_proc* folder by default contains all the processing results of T1.
- (2) The *cat* folder contains the skull stripping results (*t1\_brainmask.nii.gz*) and other intermediate files using CAT12<sup>1</sup>. *t1\_IQR.txt* contains the quality rating scores given by CAT12 and more information about the scores could be found at [CAT12 website](#).
- (3) The *freesurfer* folder contains all the files produced by FreeSurfer's *recon-all* pipeline<sup>2-7</sup>. More about these files, please refer to [FreeSurfer Wiki](#).
- (4) The *masks* folder contains files derived from *recon-all* results, including bias-field corrected image (*t1\_biascorrect.nii.gz*), brain image and its mask (*t1\_brain.nii.gz/t1\_brainmask.nii.gz*), white matter mask (*t1\_wmmask.nii.gz*), ventricle mask (*t1\_csfmask.nii.gz*), gray matter mask (*t1\_gmmask.nii.gz*) and DK+Aseg/Schaefer+Aseg Atlases (e.g., *t1\_DKAseg.nii.gz*). In addition, coronal/sagittal/axial slice pictures for these files are included for quality control purpose. More

information about DK/Aseg Atlas<sup>3,6</sup>, please refer to FreeSurfer Wiki about [Cortical Parcellation](#) and [Subcortical Segmentation](#). More information about Schaefer Atlas<sup>8</sup>, please refer to [CBIG Github Page](#).

(5) The *stats* folder contains for DK/Schaefer Atlases cortical thickness (e.g., *t1\_DK\_thickness.mean*), area (e.g., *t1\_DK\_area.sum*), volume (e.g., *t1\_DK\_volume.sum*)<sup>5,7</sup>, and for Aseg Atlas subcortical volume (*t1\_Aseg\_volume.sum*). For Aseg Atlas, the 7 bilateral subcortical regions commonly used are included.

(6) The *reg* folder contains affine registration file between T1 and MNI152 template (*t12mni.mat*), non-linear registration files between T1 and MNI152 template (*t12mni\_warp.nii.gz*), transformed files (*t12mni\_warped.nii.gz*) and pictures for checking registration quality (*t12mni.png*). The ANTs<sup>9</sup> is used for registration and more information about ANTs, please refer to [ANTs Github Page](#).

For BOLD:

(1) The *bold\_proc* folder by default contains all the processing results of BOLD.

(2) The *motion* folder contains motion-corrected file (*bold\_mc.nii.gz*), reference file for motion correction (*bold\_ref.nii.gz*), motion parameter file (*bold\_mc.matrix*), framewise displacement (FD) measure<sup>10</sup> (*bold\_mc.fd*), Friston's 24-parameter head motion model (*bold\_mc.model*), motion outliers and the threshold is FD=0.5mm (*bold\_mc.censor*), summary metrics for head motion (*bold\_mc.metric*) and picture for visualizing head motion (*bold\_motion.png*). The head motion metrics include maximum rotation (MaxRot, degree), maximum translation (MaxTrans, mm), mean FD (MeanFD, mm), the ratio between motion outliers and total volumes (OutlierRatio). AFNI's *3dvolreg* is used for motion correction, and more about AFNI<sup>11,12</sup>, please refer to [AFNI Doc](#).

(3) The *native* folder contains files in native space, including slice-timing corrected file (*bold\_st.nii.gz*), file created after motion censoring/nuisance regression/bandpass filtering (*bold\_res.nii.gz*), grand mean scaled file (*bold\_gms.nii.gz*), ReHo<sup>13</sup> (*bold\_reho.nii.gz*, 27-neighbour and Z-scored), ALFF/fALFF<sup>14</sup> (*bold\_alff.nii.gz/bold\_falff.nii.gz*, 0.01-0.1Hz, Z-scored). Slice timing correction is performed by AFNI's *3dTshift*; Motion censoring, nuisance regression, and bandpass filtering are performed in one step using AFNI's *3dTproject*; ReHo and ALFF/fALFF are calculated by AFNI's *3dReHo* and *3dRSFC*.

(4) The *reg* folder contains rigid registration file between median volume and T1 (e.g., *bold2t1.mat*), transformed image (*bold2t1\_warped.nii.gz*), and picture for checking registration quality (*bold2t1.png*). The registration is based on boundary-based method<sup>15</sup> and FreeSurfer's *bbregister*. In order to combine results with ANTs, the registration file is also converted into ANTs' format using Convert3D's *c3d\_affine\_tool*<sup>16</sup>.

(5) The *masks* folder contains the whole brain mask (*bold\_brainmask.nii.gz*), gray matter mask (*bold\_gmmask.nii.gz*), white matter mask (*bold\_wmmask.nii.gz*), ventricle mask (*bold\_csfmask.nii.gz*), DK+Aseg/Schaefer+Aseg parcellation masks (e.g., *bold\_DKAseg.nii.gz*) and coronal/sagittal/axial slice pictures for these files for quality control purpose (e.g.,

*bold\_brainmask.png*). In addition, the mean signals of whole brain/gray matter/white matter/ventricle masks are calculated for trouble shooting and for nuisance regression.

(6) The *mni* folder contains files in MNI152 standard space, including fully preprocessed BOLD images (*bold\_mni.nii.gz*), ReHo (*bold\_mnireho.nii.gz*, Z-scored), ALFF/fALFF (e.g., *bold\_mnialff.nii.gz*, Z-scored). The voxel size in MNI152 space is 3mm isotropically, because the common voxel size for fMRI acquisition is about 3mm.

(7) The *stats* folder contains five subfolders. The *roicc* subfolder contains the functional connectivity matrix calculated using mean signals for DK+Aseg/Schaefer+Aseg Atlases (e.g., *bold\_DKAseg\_roicc.matrix*) and parcel size information (e.g., *bold\_DKAseg\_roicc.info*); The *vwroicc* contains the functional connectivity matrix calculated using averaged voxel-wise correlation for DK+Aseg/Schaefer+Aseg Atlases (e.g., *bold\_DKAseg\_vwroicc.matrix*) and parcel size information (e.g., *bold\_DKAseg\_vwroicc.info*); The *reho* subfolder contains the mean ReHo for DK+Aseg/Schaefer+Aseg Atlases (e.g., *bold\_DKAseg\_reho.mean*) and parcel size information (e.g., *bold\_DKAseg\_reho.info*); The *alff* subfolder contains the mean ALFF for DK+Aseg/Schaefer+Aseg Atlases (e.g., *bold\_DKAseg\_alff.mean*) and parcel size information (e.g., *bold\_DKAseg\_alff.info*); The *falff* subfolder contains the mean fALFF for DK+Aseg/Schaefer+Aseg Atlases (e.g., *bold\_DKAseg\_falff.mean*) and parcel size information (e.g., *bold\_DKAseg\_falff.info*). The parcel size information file contains the parcel index (INDEX), label (LABEL), total voxel counts (TOTAL), non-zero voxel counts (NZERO), and coverage fraction (FRAC=NZERO/TOTAL). As BOLD images usually show signal loss in some regions (e.g., orbitofrontal cortex and medial temporal lobe) due to magnetic susceptibility, it is useful to check the parcel coverage for quality control.

For DWI:

(1) The *dwi\_proc* folder by default contains all the processing results of DWI.

(2) The *reg* folder contains the B0 image (*dwi\_b0.nii.gz*), registration file between B0 image and T1 (*dwi2t1.mat*), transformed image (*dwi2t1\_warped.nii.gz*) and picture for checking registration quality (*dwi2t1.png*). Boundary-based method and FreeSurfer's *bbregister* are used for registration.

(3) The *masks* folder contains whole brain mask (*dwi\_brainmask.nii.gz*), DK+Aseg/Schaefer+Aseg Atlases parcellation masks (e.g., *dwi\_DKAseg.nii.gz*) and pictures for quality check (e.g., *dwi\_brainmask.png*);

(4) The *eddy* folder contains file after eddy current correction/motion correction/outlier replacement (*dwi\_correct.nii.gz*), which is performed using FSL's *eddy\_openmp*<sup>17,18</sup>. *dwi\_correct.CNR* contains the contrast-to-noise ratio after correction for each shell, which could be used for quality check. More about FSL<sup>19</sup> and *eddy\_openmp*, please refer to [FSL's Eddy Page](#).

(5) The *dtifit* folder contains the FA/MD/AD/RD measures after diffusion tensor model fitting (e.g., *dwi\_FA.nii.gz*), FA/MD/AD/RD measures transformed in MNI152 space (e.g., *dwi\_mniFA.nii.gz*) and picture for quality control (*dwi\_fa2mni.png*). The registration files

(*dwi\_fa2mni.mat/dwi\_fa2mni\_warp.nii.gz*) between FA and FA58\_FMRIB template are created by FSL's *flirt*<sup>20,21</sup> and *fnirt*<sup>22</sup>. If multi-shell (multiple non-zero b-values) data is provided, the smallest non-zero b-value volumes are extracted for diffusion tensor fitting. The b-values change within 100 are treated as the same b-value. Diffusion tensor model fitting is performed using FSL's *dtifit*.

(6) The *bedpostx* and *probtrackx* folders contain the files for probabilistic tractography, which is performed using FSL's *bedpostx* and *probtrackx*<sup>23-25</sup>. More about these files, please refer to [FSL's FDT Page](#).

(7) The *stats* folder contains two subfolders. The *dti* folder contains the mean FA/MD/AD/RD for JHU Label/Tract Atlases (e.g., *dwi\_JHUlabel\_FA.mean*), and parcel size information file (e.g., *dwi\_JHUlabel\_FA.info*). More about JHU Atlas<sup>26,27</sup>, please refer to [FSL's Atlases Page](#); The *probtrackx* folder contains the structural connectivity probability matrix for DK+Aseg/Schaefer+Aseg Atlases (e.g., *dwi\_DKAseg\_prob.matrix*) and parcel size information file (e.g., *dwi\_DKAseg\_prob.info*). The structural connectivity probability matrix is calculated by normalizing the streamline counts by the parcel size, and averaging the normalized matrix and its transpose.

## 6. How to cite PhiPipe?

If you use PhiPipe in your work, you should cite our introductory paper about PhiPipe<sup>28</sup>. Also you need to cite the related softwares, on which PhiPipe is dependent.

## 7. Versions and (Major) Updates

v1.2.0 (2022-02-25)

- \* Add CAT12 for T1 skull stripping and quality check
- \* Include Schaefer Atlas for T1/BOLD/DWI processing
- \* Use FA-based registration to transform diffusion tensor measures into MNI152 space
- \* Merge left- and right-hemisphere measures into one file for T1 processing
- \* Rename files and folders for consistency and clarity

v1.1.0 (2020-07-31)

- \* Change probabilistic tractography normalization by using parcel size
- \* Add slice timing correction using custom file (for multi-band acquisition)
- \* Use averaged voxel-wise functional connectivity (FC) to compute FC matrix

v1.0.0 (2020-03-31)

- \* First release

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