Atlas-based Imaging Data Analysis pipeline for functional and structural MRI Data

$egin{array}{l} { m AIDAmri} \\ { m v2.0} \end{array}$

Code: Leon Scharwächter, Niklas Pallast, Michael Diedenhofen, Victor Vera Frazão, Marc Schneider, Markus Aswendt Manual: Leon Scharwächter, Niklas Pallast, Tim Fleiner, Victor Vera Frazão, Marc Schneider, Markus Aswendt

> Status: January 2024 Department of Neurology University Hospital Cologne

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1 Introduction

The Atlas-based Processing Pipeline for functional and structural MRI data (AIDAmri) was developed for automated processing of mouse brain MRI. AIDAmri works with T2-weighted MRI (anat), diffusion weighted MRI or diffusion tensor imaging (dwi), resting-state functional MRI (func) and the t2map values (t2map). The Allen Mouse Brain Reference Atlas (ARA, CCF v3) is registered on each of these MRI data sets and is used to analyse regions of interest. Furthermore, the regions of the ARA are used as seedpoints for the connectivity and activity matrices. The lib User-defined ROIs and masks can be generated separately and used for analysis, e.g. stroke lesion masks and peri-infarct regions. AIDAmri comes with different atlas and template versions, which are necessary for the registration to work (Figure 1): a) annotation 50 changed anno: original ARA CCF v3 labels (regions with grey values > 100,000 changed to new values starting with 2000), b) anno volume 2000 rsfMRI: atlas from a) with reduced number of atlas regions by selective region fusion, 96 regions in total, split between hemispheres (right side +2000), c) same as in b) but no split, d) same as in a) but split, e) original ARA template with 50 um isotropic resolution,

f) custom-made MRI template. For the complete list of atlas labels see: ${\tt annoVolume+2000_rsfMRI.nii.txt}$

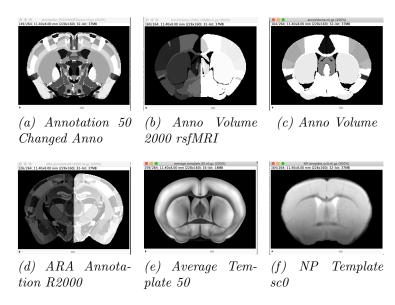


Figure 1: Atlases included in the /lib folder.

2 Installation

AIDAmri is distributed as a Docker image. If you prefer the built-in installation instead, see the legacy installation section. We highly recommend the usage of the Docker image.

2.1 Prerequisites

The following things are required to launch your AIDAmri instance.

- Docker engine (click here)
 - Getting started tutorial for Docker
- (Windows only) Bash subsystem, e.g. Git BASH
- at least 10.6 GB free disk memory

We advise you to get comfortable with Shell/command line interface (CLI) usage. The Ubuntu webpage provides tutorials such as this. Download or clone our repository:

git clone https://github.com/aswendtlab/AIDAmri.git

2.2 Docker usage

This guide introduces the usage of Docker-based containers of the AIDAmri tools for Unix/Linux-based systems (i.e. Linux and MacOS). Hence, the commands shown are written for as such and you may copy the commands into your shell including backslashes as they indicate line breaks. As mentioned in the previous section, Windows user may use a subsystem like Git BASH to use the software. You may also use the Docker Desktop application to get access to our Docker image.

2.3 General overview

The AIDAmri pipeline is containerized and structured as depicted in figure 2. The Dockerfile located in our repository provides the installation routine

for every required dependency. the docker build command constructs the image, i.e. the installed software on your system. The docker run command creates an runnable instance of this image, called a container. The container provides an interface (CLI). It can be accessed by directly attaching to an interactive interface that lets you input the AIDAmri commands within the isolated file system of the container or via the docker exec command from your host shell. How to build and use the pipeline is explained in the following sections.

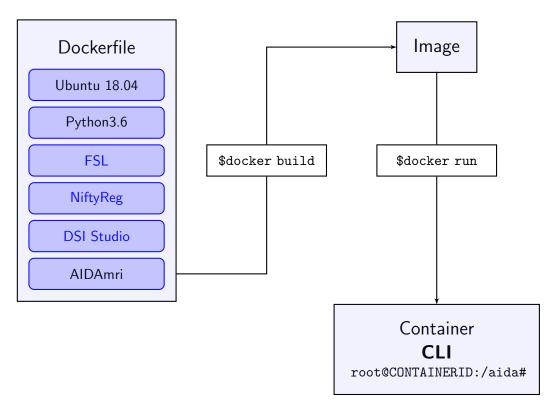


Figure 2: Docker architecture draft. The blue boxes within the Dockerfile box depict the main content layers. The boxes preceded with an \$ are command line codes. Click on texts within the boxes for further information.

The container follows a basic Ubuntu 18.04 system (see figure 3), meaning that the root directory is called "/". To share a volume between the host system and the container, we commonly use the bind mount function (see section 2.5 for further information). Please note that the mounted volume is assumed to be located in the root directory. When referring to it while in the

container, one needs to refer to it by using the path given at mounting, in this case /<MOUNTED DIRECTORY>. This path likely will be different on your host system.

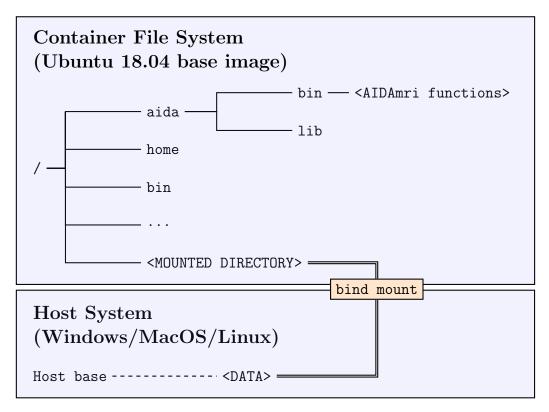


Figure 3: General structure of container file structure. The paths are constructed from left to right (e.g. the absolute path of the bin folder in aida would be "/aida/bin". Keep in mind that "/" is its own directory. The <MOUNTED DIRECTORY> and <DATA> directories are the same but can be named differently, depending on how it was named when mounted.

2.4 Creating image

To initiate the image building process, open your shell to grant yourself access to the command line interface (CLI). Change your directory to the cloned GitHub repository.

cd PATH/TO/AIDAmri

You can check the folder contents by using the ls command. A file named Dockerfile, as well as the fslinstaller_mod.py, a bin/ and a lib/ folder should be located in this directory. Then, launch the docker daemon to build the image:

```
docker build -t aidamri:latest -f Dockerfile .
```

The created image is a template for running so-called containers (see the below section) and instantiating the pipeline. Be aware that the period at the end is part of the command and refers to the corresponding directory. The -t flag calls for the name and the tag that you wish to give your image, in this case it is called 'aidamri' and tagged 'latest'. You may change name and tag to your liking, but keep in mind to change them accordingly in later steps that invoke the image. The -f tag calls for the Dockerfile in the current directory. Let the process run. Docker desktop should show you the image within the image tap once it is built.

You only need to run the building process once initially or after updating the github after new changes were made. If an update occurred, the building process will only update those layers that were changed, so the process will not take as long as the initial build.

2.5 Running container and mount data

Before running a container, make sure you know where exactly your data you wish to process is located on your host system. The container will be an instance written from the built image and serves as an environment for you to use the AIDAmri pipeline. To run the container, enter the following command in your command line:

```
docker run -dit \
--name aidamri \
--mount type=bind,source=PATH/TO/DATA,target=/aida/DATA \
aidamri:latest
```

The first flag, -dit starts the container as a detached mode, hence the d, as well as an interactive mode, that allows you to actively use this environment, hence the it. Alternatively, you can directly enter the container environment by only using the -it flag. With the --name tag you give your container a name, in this case it is called "aidamri". Note, that the image name and the container are named individually. It is recommended to give your

container a different name from the image to avoid confusion. Note further that if you wish to use more than one instance of running containers (e.g. to process multiple datasets simultaneously) you need to name each container differently.

Binding mounts create a reference to a given directory, allowing the container to access and transmute data on the host system. In this case, it should allow the pipeline to process your MRI data without copying or re-allocating your data. The --mount flag with the type=bind argument allows you to grant your container access to your target directory. Type in the absolute path at the source placeholder. Do not use relative paths. Within the container environment, a working directory called aida/ was created. It is recommended to allocate your reference path within this directory by typing in the name of your data folder according to the target placeholder, i.e. /aida/DATA. You can give the target folder another name than the source directory as it still will refer to the source but it is advised to keep the name to avoid confusion. Be aware not to place any spaces between the commas. Pass the name and tag of your image, i.e. here aidamri:latest at the end of the command line. After initializing an ID will appear and the Docker Desktop app should show the running container. You can also check whether the container is running by typing docker container 1s.

To enter the running container, use the following command:

docker attach aidamri

Windows user You can leave a running container without stopping by pressing CTRL+P and CTRL+Q consecutively. Alternatively, you can type in exit, however, this will stop the container. Use

docker start aidamri

to re-run the container. Type in "stop" instead of "start" if you like to stop an already running container.

When successfully attached, the shell prompt will look like the following:

root@<SOME NUMBERS AND CHARACTERS>:/aida#

The number shows the first part of the container ID. From here, you can use the AIDAmri commands as explained in the former usage sections. As a start, change your directory to the binary folder (cd bin/) and run python batchProg.py -h to see the helping instructions of the batch processing tool and check functionality. Alternatively, you can use the docker exec command. Basically, this pipes a command that you wish to run within

the container to the running container without directly entering its interactive environment. As an example, to run batchProg help page, type in the following command.

```
docker exec -w /aida/bin aidamri \
python batchProg.py -h
```

The -w flag acts as the directory change (cd) as you input the directory where batchProg is located (/aida/bin). Afterwards, the command is entered like in the interactive shell.

2.6 Built-in installation (legacy)

AIDAmri can be installed without the Docker usage at your host machine. Be advised that the installation process is tedious and error prone due to the different dependencies and their installation processes.

1. Download the folders /bin and /lib by using this link. /bin and /lib should be located in the same directory. Alternatively, clone the repository:

```
git clone https://github.com/Aswendt-lab/AIDAmri
```

The folder /bin contains the python scripts necessary for all preprocessing steps. The folder /lib contains several information about six atlases. Please do not conduct any changes to these files as it could influence the access from the python scripts.

- 2. Download & Install the appropriate DSI-Studio and copy the install path into .../bin/3.2_DTIConnectivity/dsi_studioPath.txt.
 - On Ubuntu: if an error is raised that states that libQt6Charts.so.6 could not be found, execute the command

```
sudo apt install libqt6charts6-dev
```

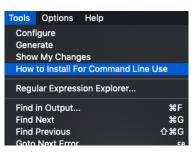
3. Download FSL installer 3.3.0 (for further information on FSL, click here. To install FSL use the following command:

```
python3 fslinstaller.py -V 5.0.11
```

4. Download and the latest version of Cmake.

- Unpack the downloaded archive and switch to the directory using cd command.
- Type in the following command to install Cmake:

./bootstrap && make && sudo make install





(a) Menu of Cmake software

(b) Install for command line use

Figure 4: Installation instructions to install Cmake.

5. Download & Install Python 3.6 or higher using Anaconda and enter the following command to install necessary packages

```
pip install nipype==1.1.2 lmfit==0.9.11 progressbar2==3.38.0 \
nibabel shutil
```

Anaconda will tell you if additional packages are necessary. We recommend to install AIDAmri in a separate Anaconda environment (see the related documentation). Alternatively, use the requirements.txt from the AIDAmri git repository to install the dependencies. Open the terminal at the folder where the requirement file is located and launch the installation.

```
pip install --upgrade pip && pip install -r requirements.txt
```

- 6. Install NiftyReg by conducting the following steps:
 - a. Generate your source folder .../NiftyReg/niftyreg_source.
 - b. Download NiftyReg from the git by replacing <path> by your personal path and enter the following command:

```
git clone \
git://git.code.sf.net/p/niftyreg/git \
<path>/niftyreg_source
```

c. Change the folder by typing in the terminal:

```
cd <path>/niftyreg_source
```

d. Type in the following command:

```
git reset --hard 83d8d1182ed4c227ce4764f1fdab3b1797eecd8d
```

e. Follow the steps described here.

3 Functions

List of functions:

- PV2NIfTiConverter: Bruker to NIfTy converter
- **T2PreProcessing:** T2w MRI pre-processing including brain extraction, bias field correction and atlas registration
- **DTIPreprocessing:** DTI pre-processing including brain extraction, bias field correction and atlas registration
- **fMRIPreProcessing**: DTI pre-processing including brain extraction, bias field correction and atlas registration
- **T2Processing**: Stroke mask calculations across all subjects per group (Incidence mapping), SNR calculations
- DTIConnectivity: Whole brain fiber tracking using DSI Studio and calculation of diffusion measures (FA, AD, RD, MD) for every brain region
- **DTIdata_extract**: Creates a .txt-file containing DTI values from all brain regions
- fMRIActivity: functional connectivity analysis for all atlas regions
- T2mapPreProcessing: functional connectivity analysis for all atlas regions

• **ROI_analysis**: Analysis of T2w, DTI, and rs-fMRI with user-defined atlas regions, e.g.: peri-infarct regions around the stroke lesion

All program examples are only listed with the mandatory input parameters. For more details/help, call python .../python <command> -h. The command line examples are given with the identifier testData<No.> .nii.gz and can be identically applied to other data. The test data is freely available: https://doi.org/10.12751/g-node.70e11f.

After a successful download, you can choose to either process single files manually or automate the processing for the whole dataset. In both cases, processing includes file conversion from the raw Bruker format into the NIfTI format, several preprocessing steps and registration with the Allen Brain Reference Atlas. The functions in /bin are named according to the MRI sequence to be processed (T2, DTI, fMRI). Additionaly it is important to process your T2 data first in order for the Preprocessing of DTI, fMRI and T2map to work.

4 Batch processing

AIDAmri provides functions for data conversion as well as processing for data batches. Complete processing requires two scripts: At first conv2Nifti_auto.py creates a new project folder, converts all files to the NIfTI format and stores them in the new project folder, batchProc.py then applies pre-processing steps and the registration with the atlas. Remember that our test data set already is converted into the NIfTI format. In this case only the second script needs to be applied. In general, the raw (Bruker format) data needs to be in the following structure for the first script to work: projectfolder/days/subjects/

To convert the whole project folder into the NIfTI format, open the terminal and change the directory to the /bin folder of the AIDAmri installation using

cd <path to AIDAmri>/bin

Enter a similar line as in the example below to start the first script (Bruker to NIfTI conversion).

Example:

python conv2Nifti_auto.py -i /path/to/raw_dataset -o /path/to/output

This script will automatically find all of your raw bruker datasets which are saved within the input path. Per default the output is saved in

```
/path/to/raw_dataset/proc_data
```

You can specify the output directory via the -o flag in the script call. After a successful Bruker to NIfTI conversion, the second script can be applied to the new project folder proc_data. The data needs to be ordered in BIDS-format likewise the output of conv2Nifti_auto.py:

projectfolder/sub-/ses-/datatype

Warning: Batch processing may slows down system depending on the CPU load-out. Use the -cpu or -e_cpu flag to specify CPU usage. Enter the command python batchProg.py -h for more information.

Example:

```
python batchProc.py -i /path/to/proc_data \
-t anat dwi func t2map -s Baseline P3 P12 -stc False
```

This script runs every necessary script for all (pre-)processing, registration and processing steps. Again, you can specify which **Datatypes -t** and **Sessions -s** to compute. Furthermore you can specify if a slice time correction should be performed on your data. Per default the -stc flag is set to False and it is optional to set this parameter. Furthermore you do not need to specify the datatypes and sessions, if no -t and no -s flag is given, every datatype and session will of every subject will be processed. Please keep in mind that the hereby executed scripts are related to each other and therefore anat always needs to be specified before dwi.

Depending on the size of your project, this process may take a while. After finishing your project folder is ready for network graph analysis, e.g. using AIDAconnect.

Further information can be accessed by python batchProc.py -h.