TOAD tutorial

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Before you start using TOAD, we recommend reading the following articles to get acquainted what with the kind of analyses are that can be conducted within TOAD :

— Jones, D. K., & Cercignani, M. (2010). Twenty-five pitfalls in the analysis of diffusion MRI data. *NMR in Biomedicine, 23(7)*, 803–820.
— Smith, R. E., Tournier, J. D., Calamante, F., & Connelly, A. (2012). Anatomically-constrained tractography: Improved diffusion MRI streamlines tractography through effective use of anatomical information. *NeuroImage, 62(3)*, 1924–1938.
— Tournier, J.-D., Mori, S., & Leemans, A. (2011). Diffusion tensor imaging and beyond. *Magnetic Resonance in Medicine, 65(6)*, 1532–1556. [PDF]

1 Before you start

1.1 Account on the UNF server

In order to use TOAD at CRIUGM, you need to create an account on the UNF's server. This account could either be an individual or a team account.
To obtain an account, or for all account-related inquiries, please contact the system administrator at the UNF André Cyr.

1.2 Command line

TOAD toolbox is command-line-based that requires entries on a terminal. Introduction to the use of command line and terminal is beyond the purpose of this tutorial. However, there are plenty of resources available for those who need to become familiar with this requirement. For instance :

— A generic tutorial
— Life hacker tutorial

1.3 SSH communication

The use of TOAD requires a remote connection between your computer and the UNF servers (even if you are working from the CRIUGM's analysis room). To do so, it is strongly recommended to use the SSH protocol, which has been installed by default on all Apple and GNU/Linux based computers. For Windows, please refer to the various external documentation listed below :

— Tutorial on Gamexe.net
— Youtube video demo

1.4 Add TOAD to your session

1.4.1 Verify if TOAD is available

In order to use TOAD, you need to source the TOAD script when you open a session. To do so, open a terminal and establish a session by connecting to one of the UNF's servers (via SSH)

```
# Replace 'username' by your UNF user ID
ssh -Y username@stark.criugm.qc.ca
```

To check the availability of TOAD, type the following command :

```
which toad
```

If the command returns a path such as `/usr/local/toad/...`, you are all set. If the command does not return anything, it means TOAD is not available for your session and you will need to add it.

1.4.2 Add TOAD

If you are using TOAD on an occasional basis, you can source TOAD *each time* you connect to the server, by typing the following command line :

```
source  /usr/local/toad/etc/unf-toad-config.sh
```

Alternatively, you can add this line to your session's profile if you want TOAD to be automatically sourced upon each connection :

1. Open/create the file .bash_profile' using a text editor :

```
vi ~/.bash_profile
```

2. Switch to `edit` mode by pressing the `i` key to add text
3. Copy and paste this line to the end of the document (without the quotation marks) : 'source /usr/local/toad/etc/unf-toad-config.sh'
4. Save and quit the editor by first pressing the ESC' key and then type `:wq` (do not forget to type the colon !)
5. To allow this change to take place, refresh the computer's memory :

```
source ~/.bash_profile
```

2 Data retrieval and preparation

2.1 From the UNF web interface

The easiest and most practical way to retrieve data acquired at the Unité de Neuroimagerie Fonctionnelle (UNF) is to use the platform available at the UNF website. This platform takes care of all that is necessary to prepare and reconstruct the images from the scanner into a downloadable Dicom format. To access the site : either from **the website of the Neuroimaging unit** (Menu `Services` then `MRI Data Download`), or directly from **the download platform of the unit**

2.1.1 Data preparation

1. Before you can download the data, you need to reconstruct them into Dicom format. To do so, go to the UNF data download website https://unf-montreal.ca
2. Enter your UNF user ID and password
3. Select the data you want to download and click on `Build images` (keep the default option `tar.gz` for image compression type. TOAD will only work with this type)
4. Give a name to the dataset to be downloaded (in our example, `unf-data`), and click on `submit`

Data will be ready for download after a few moments. **Do not close** your browser window ; we will come back to it later.
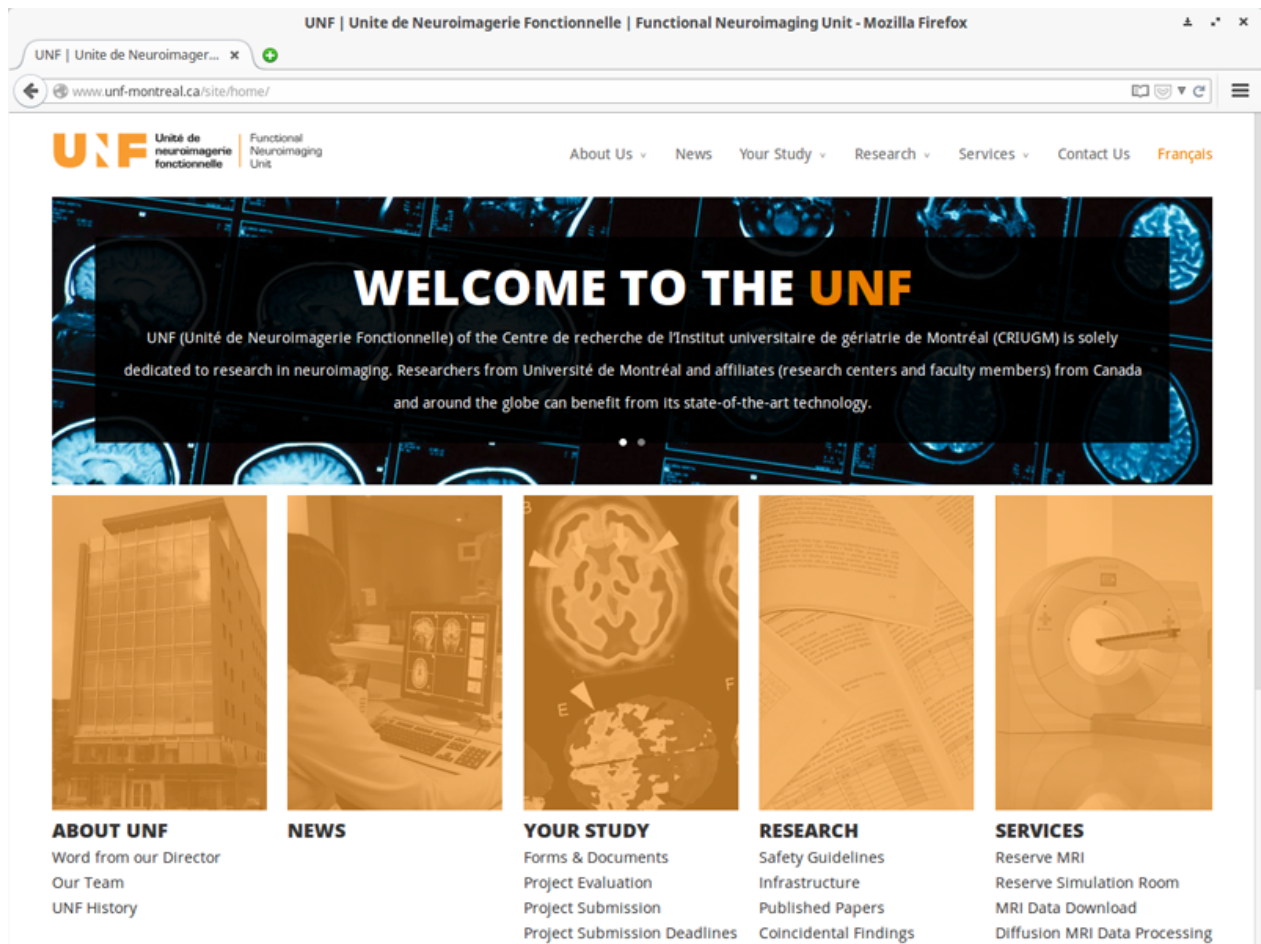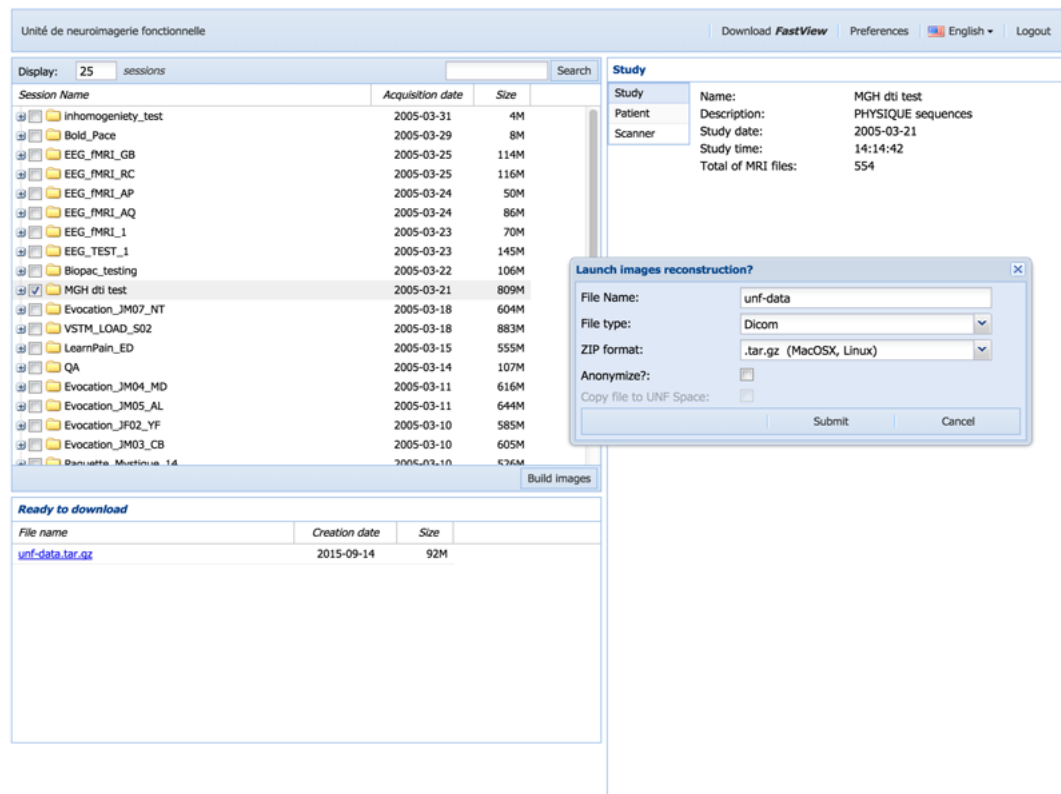
FIGURE 1 – UNF homepage

FIGURE 2 – Interface to download imaging sessions

19 mars 2016

2.1.2 Data download

In the meantime, open a terminal window and connect to one of the UNF servers (Magma or Stark) via ssh.

```
# Replace 'username' by your user ID at the UNF
ssh -Y username@stark.criugm.qc.ca
```

The server will ask for your login information

FIGURE 3 – Connexion SSH to Stark

Once connected, navigate to your data directory :

```
# Replace 'labname' by the name of the lab/group you belong to
# Replace 'username' by your user ID at the UNF
cd /data/labname/username/
```

If necessary, create a new folder for your project and go to this directory :

```
# Replace 'project_name' by the name of the folder your are naming
mkdir project_name


# To go to the new folder
cd project_name
```

Download the data prepared by the UNF platform :

1. Go back to the browser window where you are downloading your data.
2. If your data is ready for download (after clicking the `build images` button), you will see a link (in blue) with the name you had specified earlier (`unf-data.tar.gz` in our example) under the section `Ready to download`, located on the left corner of the window. The link will be available for 7 days. Copy the link address by right-clicking on the link-> **Copy link location**, in our example, it would be `http://downloads.criugm.qc.ca/user`
3. Go back to the previous terminal with the ssh session, and type the command `wget`, followed by pasting the link address :

```
# Type wget, followed by space, then right-click, choose 'Paste', or control-shift-v
wget http://downloads.criugm.qc.ca/username/unf-data.tar.gz
```

Your data are now being downloaded and will be ready to be converted by TOAD into its required format. (see section '3 Data Conversion').
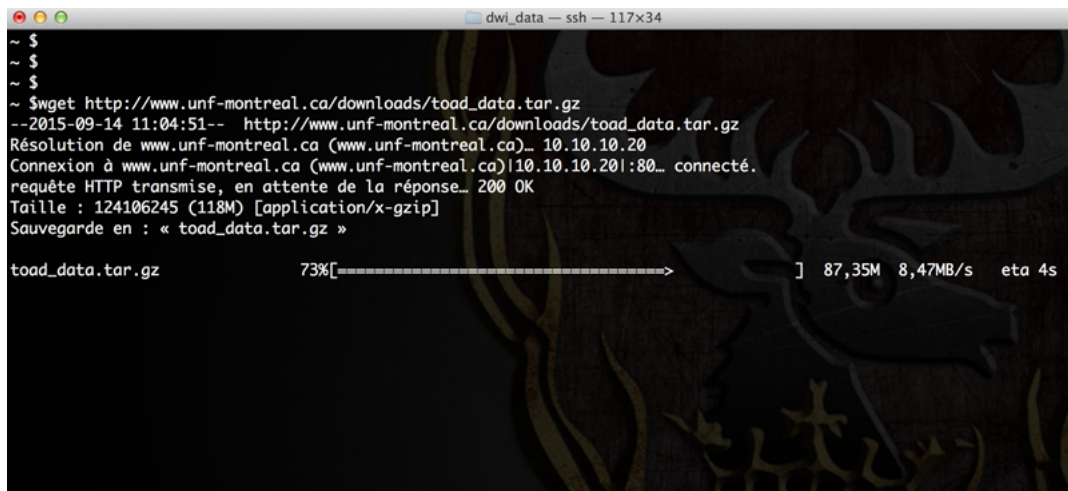
FIGURE 4 – Dowload data with WGET

2.1.3 Data conversion

ATTENTION TOAD uses its own file conversion tool `dcm2toad` to convert DICOM images into NIfTI. It is **strongly recommended** to use this tool for file conversion, because not only can it convert your data, it also generates a configuration file for TOAD. This file contains all the existing information that is unique to the raw data, and which is lost upon conversion when using other softwares.

`dcm2toad` automatically unzips and converts your data. Different options are available (see help by typing `dcm2toad -h`). By default, `dcm2toad` creates a new directory called `toad_data` where it stores all the converted files from each subject/session.

```
# Replace 'unf-data.tar.gz' by the name of your data
#   (downloaded from the UNF site)
dcm2toad unf-data.tar.gz


# To specify a target directory into which the converted files are written
#   for example 'DWI'
dcm2toad -d DWI unf-data.tar.gz
```

The software will ask you a series of questions to specify which file corresponds to which type of image (anatomical, diffusion, etc.), and to indicate the study/project ID.

One of the strong features of `dcm2toad` is its ability to manage multiple sessions/subjects simultaneously. It will first show you a list of sessions/subjects found within the downloaded data set. Subject ID followed by an asterisk * indicates that the data from that subject has been converted.

When multiple sessions/subjects share the exact same data structure, `dcm2toad` offers the option of applying the setting options chosen for the first subject to the subsequent sessions/subjects.

2.2 From another source of acquisition

2.2.1 Data type

Diffusion data analyses require at least 3 types of images for each subject :

1. **anatomical images** (T1, type MPRAGE) : anatomical mask creation, coregistration
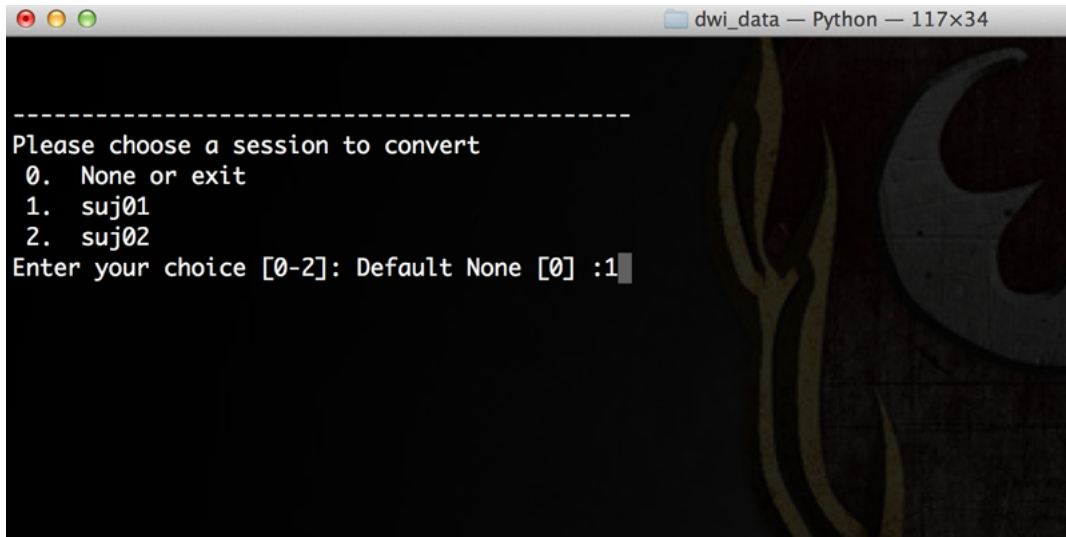2. **diffusion images** (DWI) : white matter tracts (fibre extraction)

FIGURE 5 – dcm2toad in action

3. **acquisition specifications for the diffusion images (the `b-files`) :** specifications for the acquisition of diffusion data (intensity and directions) regrouped in one (*.b) or 2 (*.bval and *.bvec) files.

Other kinds of data that can also be used by in TOAD :
— **geometric distortion/field inhomogeneity corrections** :
  — diffusion image acquired in the reverse direction of the main DWI files,
  — fieldmap image.
— **output folder from Freesurfer processing**

2.2.2 File format

For simplicity's sake, TOAD only accepts the following file formats :
— neuroimaging : **NIfTI** (.nii)
— encoding : regrouped format **MRTRIX (.b)** or separated **FSL (.bval and .bvec)**.

2.2.3 Data organization

If you have data that are already converted into NIfTI, as well as the encoding files, you can bypass the TOAD data conversion step. We recommend regrouping your data in the following manner :
— a parent folder containing all the files from your subjects
— an individual subject folder containing all the imaging files (*.nii, *.b)
Attention : *in this case, it is your responsibility to ensure that all your files have been correctly converted, and that the encoding file complies with the usual standards (strides ...). If the data comes from a 3T Tim Trio Siemens MRI scanner (like at the UNF), and you have access to the raw dicom data, we strongly recommend using the software `dcm2toad` see section Data conversion

2.2.4 File nomenclature

TOAD needs to identify which files correspond to which image. To do so, TOAD uses a prefix that is common to all the files of the same type. Similarly, all the anatomical images should start by the same prefix ; by default TOAD looks for files that start with `anat`. For diffusion images, TOAD looks for files that start with `dwi`, and for the encoding files TOAD looks for files that start with `dwi` and have `.b` or `.bval` and `.bvec` extensions. When the

anterior-posterior or posterior-anterior files are available, TOAD looks for the prefix `b0_ap` and `b0_pa`.

You are free to use any current naming system, as long as it is specified in your configuration file `config.cfg`. It must be consistent across all subjects, unless you specify a new configuration file in the folder.

2.3 Sample data set and demonstration

We suggest you download a sample dataset to discover how the pipeline works by following these steps :

```
# Connect to the UNF server
# Replace 'username' by your user ID at the UNF
ssh -Y username@stark.criugm.qc.ca

# Navigate to your data directory
# Replace 'labname' by the name of the lab/group you belong to
# Replace 'username' by your user ID at the UNF
cd /data/labname/username/

# Create a folder for your project
# Replace 'project_name' by the name of the project
mkdir project_name

# Go into the new folder
cd project_name

# Download the sample data set
wget http://unf-montreal.ca/downloads/toad_dicom.tar.gz
```

3 TOAD

3.1 Running TOAD

Once the imaging data is converted, you simply have to run the command 'toad' from the folder that contains the converted files :

```
# Go to the data-containing folder
cd toad_data

# Run TOAD
toad .
```

Data preprocessing for one participant takes about 2 days to complete. Parallel processing of multiple participants or a large dataset is also possible on the UNF servers, depending on their work load at the given time.

3.2 Verifications

3.2.1 Analysis in progress

One can check the progress of the preprocessing (e.g. how many subjects have been preprocessed) on the UNF servers by typing the command 'qstat -f'.

If your analyses are ongoing, you should be able to see your username associated with the name of the participant being analyzed and with the software being used at the moment (e.g. FreeSurfer).

During processing, you can use the following command to check the quality of the different stages as they are being completed : `firefox 00-qa/index.html` (see below).

3.2.2 Post processing

Once the work is finished, you will find a new set of folders in each participant's directory. *Reminder*, by default, this folder is located in the initial project folder `toad_data`, or the folder you specified during the data conversion with `dcm2toad`.

These folders contain the dataset, masks, and images generated by the TOAD preprocessing pipeline. The results can be quickly verified thanks to QA. The set of folders for each participant should ressemble the following table :

Folder name	Type of data
00-backup	Raw data (Nifti)
00-qa	Quality Assessment - HTML summary pages
01-preparation	Image reorientation, if necessary
02-parcellation	Parseg and Brodmann, left/right (Freesurfer)
03-atlas	Generation and application of atlases
04-denoising	Image denoising
05-correction	Motion correction, field inhomogeneity, etc.
05-preprocessing	
06-upsampling	Resolution upsampling
07-registration	Registration T1/DWI
08-atlasregistration	
09-masking	Mask generation
08-snr	Signal to noise ratio calculation
10-tensorfsl	Tensor reconstruction (FSL)
11-tensormrtrix	Tensor reconstruction (MRTRIX)
12-tensordipy	Tensor reconstruction (Dipy)
13-hardimrtrix	HARDI reconstruction (MRTRIX)
14-hardidipy	HARDI reconstruction (Dipy)
15-tractographymrtrix	Fiber tract reconstruction (MRTRIX)
16-tractographydipy	Fiber tract reconstruction (Dipy)
17-snr	Signal to noise ratio calculation
18-outputs	Regroups all data outputs (denoised and resampled images, tensors, fiber tracts
99-logs	Log and error files

Note : This organisation may change with the different versions of TOAD. Furthermore, the choice of certain parameters at the beginning of the pipeline, or the absence of certain files (e.g. B0 AP/PA) means certain tasks will not be executed.

The first step to verify that all analyses ran smoothly is to check that these folders have been generated for each participant. The absence of a series of folders indicates that the pipeline encountered a problem and stopped for the participant in question.

If that is the case, one may want to consult the last log file generated by TOAD. This file, `*.log`, will be located in the last folder created by TOAD, or in `99-logs`. This folder also contains a file such as `number_subject.e1111` (where 1111 corresponds to processing number attributed to the task) that combines all errors encountered during TOAD processing.

Results can be quickly verified thanks to the QA.

3.2.3 Quality Assessment

TOAD offers a simple yet complete interface to explore data quality and the results obtained. To start the QA, open a web browser using the command `firefox 00-qa/index.html`. After some time, the browser will load a page containing different images associated with the QA. *Warning :* for the command to work, the SSH session had to be launched with `-Y`to allow for graphics.

```
ssh -Y username@stark.criugm.qc.ca
```

The browser will open a welcome page that contains a link to each completed task. You will also find the main parameters and images necessary to evaluate data quality and check for proper pipeline functioning.

For example, you can observe the effect of the correction with before/after images, look at the signal to noise ratio, etc.

In case of errors, you fill find more information in the log folder situated in each task's folder.

```
# Replace 'toad_data' with the name of the folder used during the conversion
cd toad_data/subject_name/99-logs

# List available logs
ls

# To check a log file (results.log in this case)
vi results.log
```

4 Advanced usage in case of an error

4.1 TOAD options

It is possible to check for different TOAD options by simply typing `toad` in the terminal. You will see a list of options to be added to TOAD to run certain tasks, to add certain parameters, or to avoid different steps.

The two following command lines may be particularly helpful.

4.2 Run TOAD for a single participant

`toad foldername` where 'foldername' is the name of the participant's folder

4.3 Reset data

TOAD saves all raw data (following the `dcm2toad` conversion, for example), and can return to this stage by using the command : `toad -r ..`

You can also reset the data of a single participant using the command : `toad -r foldername` where 'foldername' is the name of the participant's folder.

4.4 Error example

You may encounter errors during data processing. For example, the default algorithm used (NLMEANS) may not be compatible with your dataset. In this case, even though the analysis will start running, it will need to be terminated.

To do this, open the terminal at the location of your work folder :

1. Check whether there are ongoing analyses using the command : `qstat -f`

2. Stop the analysis in progress per participant using the command : `qdel #id` where "#id" corresponds to the processing number attributed by qstat.

3. Reset to the original data using the command : `toad -r` . A warning will appear stating the process is locked. You will need to select `r` and confirm so that TOAD removes this lock to reset the data.

4. Change the necessary information in your data or in the configuration file (e.g. add a file "config.cfg" in the work folder with the option `algorithm=lpca` in the `[denoising]` section).

5. Restart TOAD using the command `toad` .

For more information, **consult the documentation** available for each task in the TOAD pipeline.