MASSACHUSETTS GENERAL HOSPITAL

Granger Processing Stream

Manual for version 1.9

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This document outlines the purpose and operation of the Graphical Processing Stream as produced by A. Conrad Nied in the lab of David W. Gow

Contents

Acknowledgements and Overview

The Granger Processing Stream (GPS) was developed by the Gow Group in the Department of Neurology at the Massachusetts General Hospital and the Athinoula A. Martinos Center for Biomedical Imaging with support from the National Institute of Deafness and Communicative Disorders (R01 DC003108). It also benefited from the support of the MIND Institute and a NCRR Regional Resource Grant (41RR14075) for the development of technology and analysis tools at the Martinos Center. Many people contributed to the development of this stream including David Gow, Jennifer Segawa, Ricky Sachdeva, Corey Keller, Mark Vangel, Reid Vancelette, Bruna Olson, David Caplan and Seppo Ahlfors. Conrad Nied made invaluable contributions to the approach, and is responsible for coding and developing GPS's graphic user interface and for writing most of this manual.

We developed it to address some of the inherent inferential limitations of behavioral and BOLD imaging techniques. Our goal was to develop an analysis stream that respects the logic and assumptions of Granger causality analysis. Our approach and its motivation is outlined at more length in Gow & Caplan (2012). Granger analysis is built on an inference explored by Norbert Wiener (1956) and later made practical by Clive Granger (1969) that causes both precede and uniquely predict their own effects. The mathematical logic is simple. To understand what drives a target signal (e.g. activation timecourse for some brain region), one can measure all non-redundant, potentially causal signals and apply them to develop a mathematical prediction about the future course of that signal. This prediction will inevitably be wrong. Mathematical models quantify just how wrong it is using an error term. In Granger analysis, this prediction process is then repeated using all measured signals except one. This will produce another error term. The eliminated signal is said to Granger cause the predicted signal if dropping it from the prediction causes a meaningful increase in the error term.

Granger analysis and its practical implementation rests on four main assumptions. These are all directly addressed in GPS. They are:

Exhaustive Measurement

In its strongest form, Granger analysis requires the measurement of all signals. If all signals are measured and applied to prediction Granger analysis should be immune to spurious causation artifacts. This assumption is unrealistic in virtually all applications of Granger analysis (and is essentially ignored in bivariate approaches). Recognizing the limits of neuroimaging data, and the practical consequences of applying factoral analysis to very large data sets, we developed several automated approaches to ROI selection that allow the user to identify a set of candidate ROIs based on changed activation relative to pre-trial baseline measures. Using our standard parameter settings we typically perform analyses over networks comprised of 15 – 35 ROIs. Users have the freedom to vary these parameters to produce more or less exhaustive sets, but should recognize that the use of smaller sets may expose users to an increased risk of spurious causation.

Non-redundancy

If two or more signals are identical (carry the same information), the logic fails because removing one will result in no net loss of information. We address this assumption through an automated ROI selection algorithm that limits the similarity between redundant ROIs. When two signals are too similar, the candidate ROI with the strongest activation is typically retained.

Stationarity

In its original mathematical formulation, Granger analysis also assumes that all signals are stationary (show no change in variance or central tendency over the time that is modeled). Neural signals, and especially event-related neural activity is inherently non-stationary, and so this assumption creates significant challenges when Granger analysis is applied these data. We address this assumption through the use of time-varying multivariate autogression modeling techniques. Because these approaches create a new model at each timepoint, there is no need to assume stationarity. We rely on a Kalman filter technique developed by Milde et al. (2010) for all analyses. One of the bonuses of this approach is that it makes it possible to quantify the strength of Granger causation effects independently at each timepoint.

Proper Data

GPS relies on MR-constrained source space reconstructions of MEG/EEG activity over all cortical surfaces. We do this for several reasons. From a mathematical standpoint, the timeseries analyses needed to perform predictive modeling require a large number of datapoints. Kalman filter techniques were developed (also with significant input from Norbert Wiener) for the analysis of systems of noisy data and operate through an iterative process of prediction and correction. When first applied, Kalman filters require some period of time to settle before they provide reliably strong prediction. As a rule of thumb this process may require at least 100 timepoints. From a neuroscience perspective, the purpose of these analyses is typically to track events that may take place over the order of tens of milliseconds. For these reasons, it is essential to apply these analyses to high temporal resolution data (e.g. MEG/EEG). We do not recommend the application of GPS to lower temporal resolution measures (e.g. BOLD signal). For the purposes of interpretation, it is also essential to observe as much of the brain as possible (to identify all potentially causal signals) and to be able to relate activity to interpretable localized processors. MR-constrained MEG/EEGG data support reconstructions over all cortical surfaces, and provide spatial resolution that typically places sources within the range of a typical Brodmann unit. Advances in multimodal imaging should improve this spatial resolution over time, but at present the resolution is sufficient to relate measures of effective connectivity to analyses of functional localization based on BOLD imaging and the analysis of the effects of localized pathology.

Goals

Given appropriate funding, we hope to continue to develop and refine GPS. We are not currently able to provide full support. For now, we hope to help identify a community of users who can trade expertise. If you use GPS please let us know (gow@helix.mgh.harvard.edu).

Citation

For the time being, all citations of GPS should cite this manual, and the overview of our approach provided in:

Gow, D.W., & Caplan, D. (2012). New levels of language processing complexity and organization revealed by Granger causation. **Frontiers in Psychology**, 3, 506. doi: 10.3389/fpsyg.2012.00506

The Kalman filter technique we use comes from:

Milde, T., Leistritz, L., Astolfi, l., Miltner, W.H.G., Weiss, T., Babiloni, F., & Witte, H. (2010). A new Kalman filter approach for the estimation of high-dimensional time variant multivariate AR models and its application in analysis of laser-evoked brain potentials. **NeuroImage**, 50, 960-969. Doi: 10.1016/j_neuroimage_2009.12.110.

Licensing

GPS is a GUI-based program written by A. Conrad Nied based on analyses developed by David Gow and members of his lab at the Massachusetts Hospital to automate MNE and FSL analyses of MR-constrained MEG/EEG data and to perform Kalman filter based Granger analyses of those data. Copyright © 2014. A. Conrad Nied and David Gow.

Chapter 1: Introduction

The Matlab program suite was originally made to simplify the analysis process. As more routines were incorporated the program grew and more user interfaces were added to the library. The software contains many functions contributed to by many other researchers at the Athinoula A. Martinos Center for Biomedical Imaging.

There are 3 design principles in the formation of this program suite: Accessibility, Visualization, and Reproducibility.

Accessibility

All researchers regardless of specific programming background should be able to analyze their data using software routines. By creating an interactive, visual environment, more people are able to engage in the science.

Visualization

Data, not just the final result,should be easily visualized . At the end of the an analysis, the final result may look defensible, but problems in middle steps can invalidate results. Thereby, instead of operating routines as black boxes, GPS aims to provide visual feedback for each stage of the result.

Furthermore, GPS provides and links to many interactive environments in which one can explore their data and check for consistency.

Reproducibility

Due to the complex nature of brain imaging research, variance can be introduced at many stages. Variance can be caused by subjects and experimental paradigms, but also small changes in conducting an analysis, such as changing which channels to exclude for a subject or selecting regions of interest that are a little off between subjects. After so many transformations of the data, deviations in protocol can drastically change the final result.

Thereby, by providing a framework to organize a study and a system that is as automated as possible, a stable protocol can be followed good results can be attained .

Chapter 2: Setup

Operating System

The interface is compatible with Mac OS X and Linux. However, it was built on a Linux machine (Cent OS) and is thereby optimized for operation on Linux. Some computer configurations may case graphical glitches with the Matlab graphical user interface (GUI) routines. These mostly affect the alignment of certain interface elements but it will not affect the data.

Software

Three programs are necessary in order to run the Graphical Processing Stream. Martinos Center users already have this software provided.

Matlab

The processing stream is run out of Matlab. Additionally, it uses a number of Matlab toolboxes, packages of functions necessary for the interface. Some of the toolboxes may need to be acquired separately. In order to run all aspects of the processing stream one will need:

- Matlab 7.11 or later and necessary toolboxes:
    - Image Processing Toolbox
    - Distributed Computing Toolbox
    - Statistics Toolbox

http://www.mathworks.com/products/matlab/

Freesurfer

This program is used to process Magnetic Resonance Imaging (MRI) scans. It reconstructs cortical surfaces from raw brain images. The analysis stage called MRI (in Chapter 5.2) utilizes many Freesurfer commands. Freesurfer is crucial for GPS to use the Minimum Norm Estimates toolbox in constructing cortical and skull maps. See the websites for more information:

Main portal:	http://surfer.nmr.mgh.harvard.edu/
Download:	http://surfer.nmr.mgh.harvard.edu/fswiki/DownloadAndInstall

Additional Freesurfer Matlab functions are bundled with the GPS routines. These commands import the Freesurfer data in order to render images of the brain.

Minimum Norm Estimates

Matti Hämäläinen’s Minimum Norm Estimates software creates estimates of cortical activity by combining Freesurfer cortical surfaces with MEG/EEG signals. GPS started as shell program, interacting with the MNE routines. At their current state, most functions in GPS are independent of MNE but MNE was instrumental in designing the functions.

http://www.martinos.org/mne/

Setup Routine

After these software packages have been installed and loaded into the environment, the processing stream can be opened in Matlab. Setting up the environment can be done easily using a tsch or bash script, such as the tsch script provided below. All phrases in '< >' signs refer to variables that should be indicated by the user.

```
# Set the folder where GPS is located
setenv WORKHOME <GPS directory>
cd $WORKHOME

# Load the Freesurfer software
setenv FREESURFER_HOME <Freesurfer directory>
source $FREESURFER_HOME/SetUpFreeSurfer.sh
setenv FSFAST_HOME $FREESURFER_HOME/fsfast
setenv MNI_DIR $FREESURFER_HOME/mni
# setenv FSL_DIR <FSL software directory>
setenv SUBJECTS_DIR <Study processed MRI directory>

# Load the Minimum Norm Estimate software
setenv MNE_ROOT <MNE software directory>
setenv MATLAB_ROOT <Matlab software directory>
source $MNE_ROOT/bin/mne_setup

# Start Matlab
matlab
```

For the users in the Martinos center in particular, use these commands:

```
# Set the folder where GPS is located
setenv WORKHOME <GPS directory>
cd $WORKHOME

# Load the Freesurfer software
source /usr/local/freesurfer/nmr-stable52-env
setenv FSFAST_HOME /usr/local/freesurfer/stable4/fsfast
setenv MNI_DIR /usr/local/freesurfer/stable4/mni
setenv FSL_DIR /usr/pubsw/packages/fsl/current
setenv SUBJECTS_DIR <Study processed MRI directory>

# Load the Minimum Norm Estimate software
setenv MNE_ROOT /usr/pubsw/packages/mne/nightly_build
setenv MATLAB_ROOT /usr/pubsw/packages/matlab/current
source $MNE_ROOT/bin/mne_setup

# Start Matlab
matlab8.0
```

In order to speed up the execution of these commands, it is recommended to save these into a shell file and create an alias for the command. For instance, if these commands are saved in the file “setup_GPS” located in the home directory, users should edit the “.cshrc” (or .bashrc) file in the home directory, by adding the line:

```
alias GPS course ~/setup_GPS
```

This will enable the user to load Matlab set with the environment for the graphical processing stream by just typing the shell command “GPS”.

Graphical Processing Stream

A processing stream is a collection of programs organized into steps that perform an analysis. The processing stream consists of four primary interface programs and a host of functions.

Acquiring GPS

GPS is hosted on Martinos Center website. You can download the repository from: www.martinos.org/software/GPS

First Time Initialization

The first time you run GPS, you will need to run a script to initialize the functions. The script is called `gps_init.m` and is located in the main directory. Run it out of Matlab. This function will ask you which directory is GPS located in, and the desired locations for the images, logs, and parameters files. It will optionally clear the parameters folder, so if you are starting over click yes, otherwise click not to clear the parameters folder. Staring over will remove all images in the images directory so make sure you have backed up any images.

Starting it up

After setting up the environment, the user interface can be started up by typing the command GPS in Matlab. This command will add the GPS functions to the Matlab path and bring up a dialogue for the user to choose which interface to open as seen in Figure 2.1. This menu can be reopened at any time by typing GPS again.

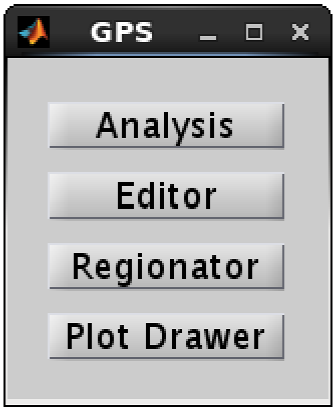


Figure 2.1

Organization

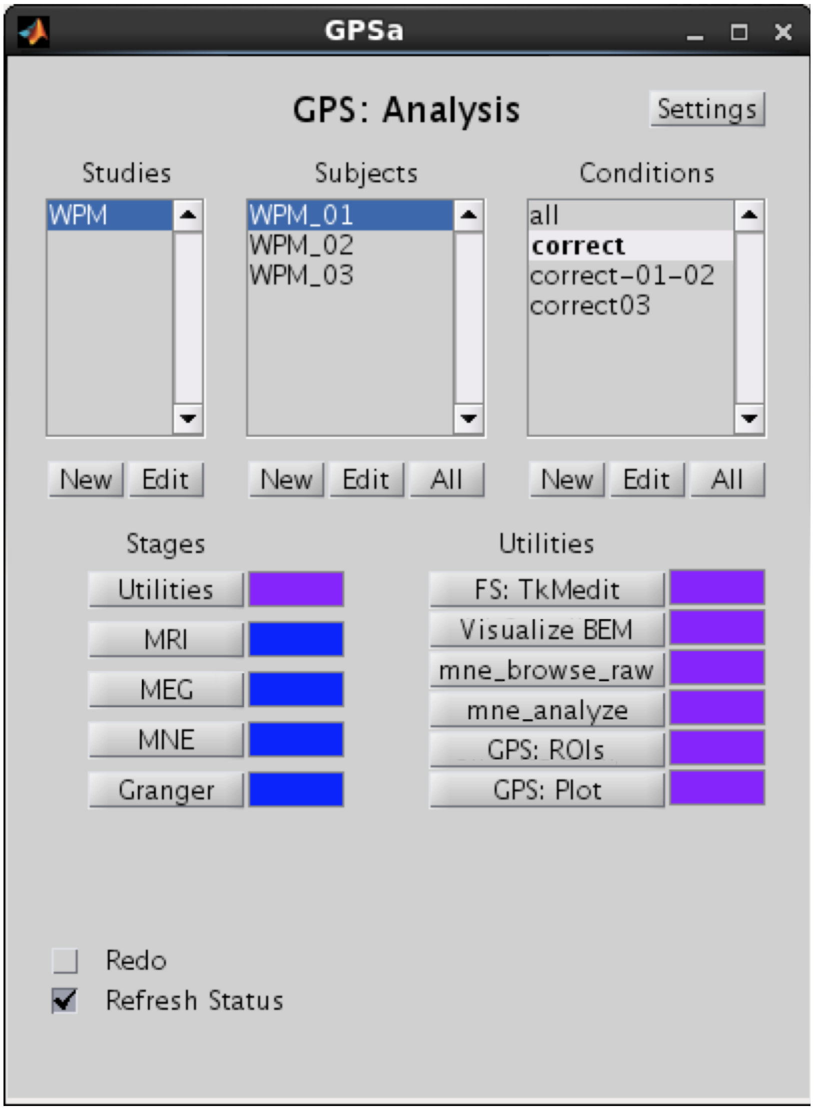
The GPS directory contains four folders and the starter GPS functions.

The functions folder contains all of the Matlab routines used by the GUIs and analysis. Images made specific for Matlab sessions are put in the images folder. The image folder pictures are organized by date. The logs folder contains records for the analysis routines for each study. The parameters folder contains all of the analysis parameters such as timing and thresholds. These parameters can be edited using the structure-editing interface as described in Chapter 6.

The scans, intermediate analyses and results for the studies are saved in a separate folder for the study. Images that are permanent records for analysis are saved in the study folder, but intermediate or interface-driven images are saved in the GPS/images folder (or other if you specified).

Chapter 3: Analysis Interface

For the sake of generalizing and accessibility, the analysis functions have been streamlined and put in one interface.



☐ Redo
☑ Refresh Status

Figure 3.1

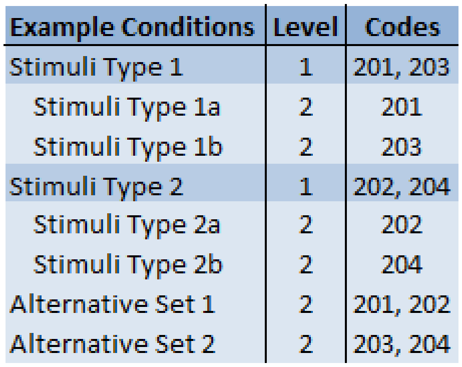
Selecting Datasets

The top of the interfaces has three lists. The first list enables the user to select a study and then the study's subjects and conditions' subsets can be modified. Once a study is selected, many interior variables are changed and analysis functions may change. The *new* and *edit* buttons can be used to add new studies and open the structure editing interface to edit parameters of the study selected.

Subjects and conditions are specified on the other two lists. Multiple items can be specified using shift (for continuous selection) and ctrl (for discrete selection). The ‘All’ buttons under each list will select all elements in that list. Every time the selection of the study, subject, or condition is altered, the program will reload certain elements and refresh the status bars.

Conditions

An important design consideration is the organization of trials into sets. For instance, the investigator may want to look at the data in one combination initially, but then combine or split up the data later. Each relevant combination of data should be analyzed as a different condition.



Example Conditions	Level	Codes
Stimuli Type 1	1	201, 203
Stimuli Type 1a	2	201
Stimuli Type 1b	2	203
Stimuli Type 2	1	202, 204
Stimuli Type 2a	2	202
Stimuli Type 2b	2	204
Alternative Set 1	2	201, 202
Alternative Set 2	2	203, 204

Figure 3.2

Primary v Secondary Conditions

One important distinction is the differentiation between primary and secondary conditions. Certain analyses may call for straightforward divisions of the analysis, like all trials into sets A and B. However, later analyses may ask to use only some of the trials from A or splitting it into two more subsets C and D. Instead of locking the user into specific data conditions from the start, the program is meant to be run first for initial subsets. These conditions should cover all of the data, yet not overlap, because it is used in the construction of the map between cortical and sensor activity. Secondary conditions can be additional sets derived from the primary sets or novel combinations.

Further Specification

The `Settings` button opens a menu, shown in figure 3.3 to enable further customization of the dataset.

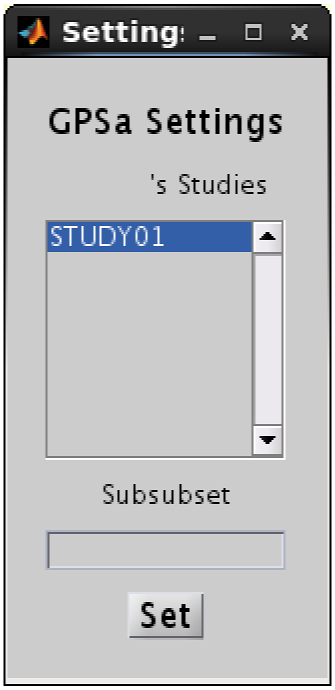


Figure 3.3

In large groups, the study list may get long so individual users can specify which studies they would like to see in the main GUI through this dialogue. This list can be changed at any time, just note that it will reinitialize the list of studies in the main window.

Stages and Functions

The lower half of the analysis interface is used to run the analysis functions. The left column lists various stages of the analysis: Utilities, MEG, MRI, MNE, PLV, and Granger. They will be detailed in Chapter 5. Clicking on one of these buttons will change the function list on the right side to the list of functions for the particular analysis stage.

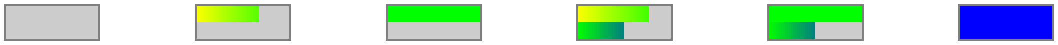
The functions show up as a series of buttons showing the progressive routines of the particular stage. Clicking on a single button will start the analysis for the selected subject(s) and condition(s). Some functions work across all subjects and/or all conditions.

Status and Override

In each function script, there is a portion of the code dedicated to determine if a function is ready to be performed and if it has been completed. The grey rectangles next to each stage and function show its progress when the “Refresh Status” checkbox is checked at the bottom of the screen – changing the selected subjects and conditions will cause the interface to recheck the existence of files on the hard drives so it could take a few seconds to show the correct status.

For certain functions, the ready/finished status of routines is determined on demand when they are called by the interface to be processed. If a function is not ready to be processed or it has already finished and isn’t repeatable, it will not run. To rerun a finished function, check the “Override” checkbox, sometimes this may require you to delete the already finished results but that case should only happen with the Freesurfer commands. The table below shows the various readiness statuses and their corresponding coloring

Not Ready	Partially Ready	Ready	Partial Ready Partial Finish	Partially Finished	Finished



Batch

The checkboxes next to stage and function names are included to aid in the serial processing of many functions. If multiple items in the function list are selected and the “Batch” button is clicked, the program will attempt to do each function selected for each selected subject and condition as necessary. If a process fails covertly it will detect the next function is not ready and won’t proceed for that particular dataset (subject/condition). If a process bugs the interface it will halt the execution.

Function Management

For the Analysis Interface, functions are organized by stages in their directories under `functions/gpsa/<stage>/…` Instead of keeping a solid list of functions, in each stage directory there is a program that returns the list of functions for that stage: there interface name and the program name. This file can be amended to remove or add buttons to the particular stage in the interface.

Functions can be edited for specific studies as well. For example, the event processing function of the MEG stage is customized for each study. The GUI will automatically look for functions that match the pattern <function>_<study.name>.m before it processes <function>.m

Most analysis functions are created with the framework on the following page Each function can be run from the Matlab command line with the state specified –a structure containing the fields

.study indicating the study name, .subject, and .condition, and also .dir specifying the GPS folder.

Analysis Function Layout

```
function varargout = gpsa_<function name>(varargin)
% <function description>
%
% Author: <author>
%
% Changelog:
% <date> <edits>

%% Input
[state, operation] = gpsa_inputs(varargin);

%% Prepare a report on the type of the function
if(~isempty(strfind(operation, 't')))
    report.spec_subj = <is the function subject specific?>;
    report.spec_subs = <is the function condition specific?>;
end

%% Execute the process
% If it is proper to do the function
if(~isempty(strfind(operation, 'c')))
    subject = gpsa_parameter(state, state.subject); % Get subject structure
    state.function = 'gpsa_<function name>';
    tbegin = tic;

    <function contents>

    % Add an entry to the log reflecting the processing of this function
    gpsa_log(state, toc(tbegin));

end % If we should do the function

%% Add to the report concerning the progress
if(~isempty(strfind(operation, 'p')))
    subject = gpsa_parameter(state, state.subject);

    if(~isempty(subject))
        % Predecessor: <function's predecessors>
        report.ready = <ready logical statement>;
        report.progress = <progress logical statement>;
        report.finished = report.progress == 1;
    else
        report.ready = 0;
        report.progress = 0;
        report.finished = 0;
    end
end

%% Prepare the report and output
if(nargout == 1 && exist('report', 'var'));
    varargout{1} = report;
end
```

```
end % function
```

Utilities

Before the main analysis function, this stage instead opens up external programs. The function options in the GUI are seen in figure 3.6.

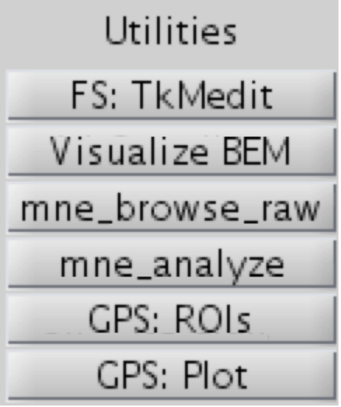
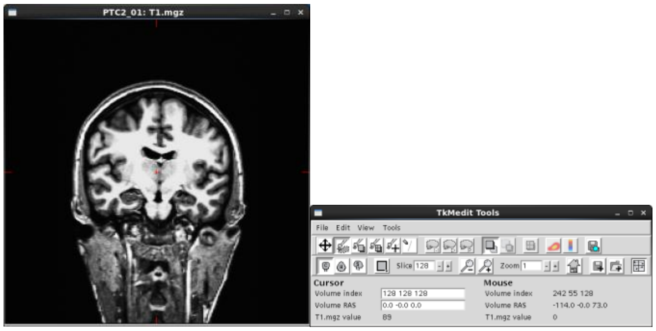


Figure 3.6: Utilities

Freesurfer’s TkMedit program can be useful in analyzing the MRI . It is also useful for double checking the processed MRI data. An example of its usage is in figure 3.7.



Slice 128

Zoom 1

Cursor

Volume index 128 128 128

Volume RAS 0.0 -0.0 0.0

T1.mgz value 89

Mouse

Volume index 242 55 128

Volume RAS -114.0 -0.0 73.0

T1.mgz value 0

Figure 3.7: TkMedit

Visualize BEM draws three-dimensional representations of the boundary element model. It will make a figure like the one shown in figure 3.8. This Matlab figure can be rotated in 3D space. The green layer shows the scalp as defined for MNE’s BEM computation. The blue layer shows the outer extent of the skull. Note that this is an approximation and portions such as the jaw may be off. The red layer shows the inner extent of the skull, and inside it the brain is shown in gray, (although usually not visable). If one layer overlaps another, there will be errors in the MNE model that computes the neural activity..

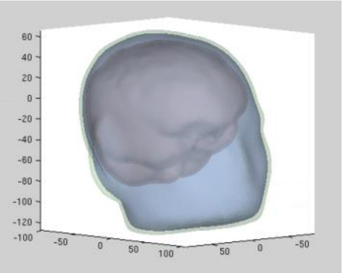
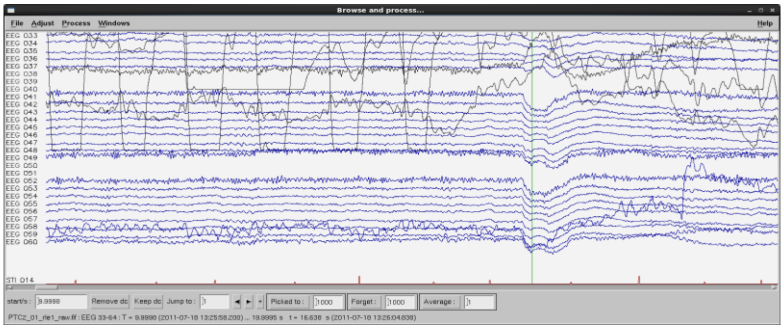


Figure 3.8: Visualize BEM

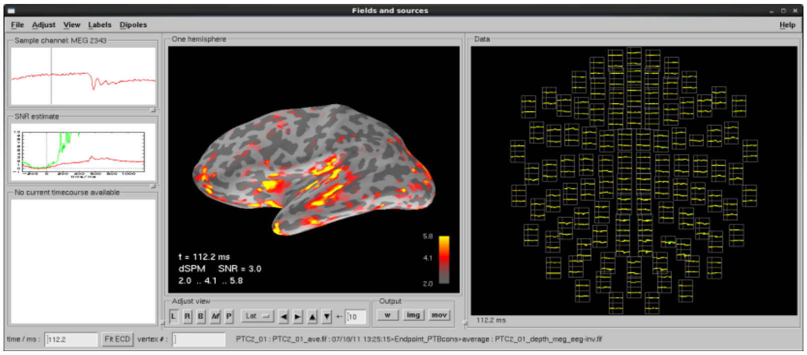
Minimum Norm Estimate’s `mne_browse_raw` and `mne_analyze` programs help in preprocessing and viewing the data after the estimates have been created. Their usage will be detailed in the MNE section.



start/s : 9.9998 Jump to : 1 Picked to : 1000 Forget : 1000 Average : 1

PTC2_01_rle1_raw.fif : EEG 33-64 : T = 9.9998 (2011-07-18 13:25:58.200) ... 19.9995 s t = 16.638 s (2011-07-18 13:26:04.838)

Figure 3.9: mne_browse_raw



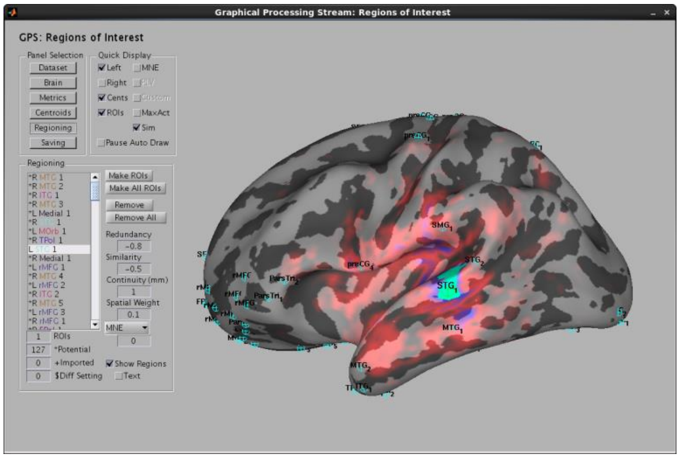
t = 112.2 ms
dSPM SNR = 3.0
2.0 .. 4.1 .. 5.8

time / ms : 112.2 vertex # :

PTC2_01 : PTC2_01_ave.fif : 07/18/11 13:25:15>Endpoint_PTBcons>average : PTC2_01_depth_meg_eeg-inv.fif

Figure 3.10: mne_analyze

The remaining two buttons open up interfaces developed along with GPS.
`GPS: ROIs` is used to automatically cluster regions of the brain based on neural activity; it is described in more detail in chapter 6.
`GPS: Plot` creates an environment to visualize granger causality, it is described in chapter 7.



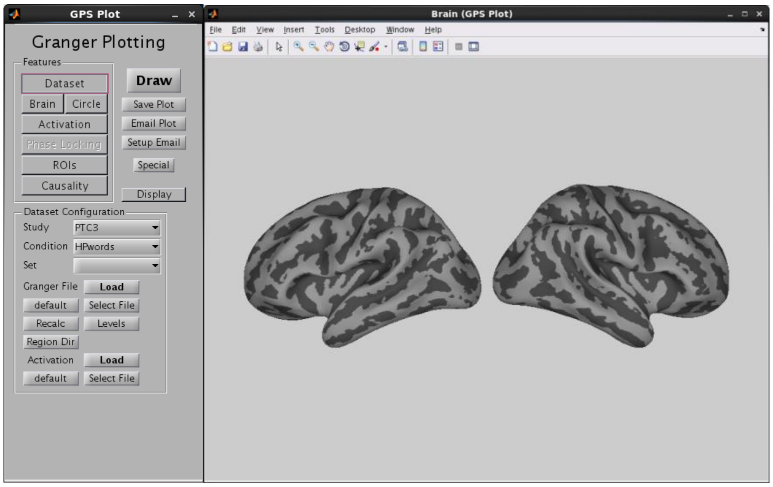
☑ Left □ MNE
□ Right □ PLV
☑ Cents □ Custom
☑ ROIs □ MaxAct
☑ Sim
□ Pause Auto Draw

*R MTG 1
*R MTG 2
*R ITG 1
*R MTG 3
*L Medial 1
*R 1
*L MOrb 1
*R TPol 1
L STG 1
*R Medial 1
*L rMFG 1
*R MTG 4
*L rMFG 2
*R ITG 2
*R MTG 5
*L rMFG 3
*R rMFG 1

Redundancy -0.8
Similarity -0.5
Continuity (mm) 1
Spatial Weight 0.1
MNE 0

1 ROIs
127 *Potential
0 +Imported
0 $Diff Setting
☑ Show Regions
□ Text

Figure 3.9: GPS ROIs



Study PTC3
Condition HPwords
Set

Figure 3.10: GPS Plot

Chapter 4: Analysis Routines

4.1 Magnetic Resonance Imaging

The MRI stream is largely automated. It is broken down into sections based on the functions run. Steps 2 to 9 are automated so they can be easily batch ran together.

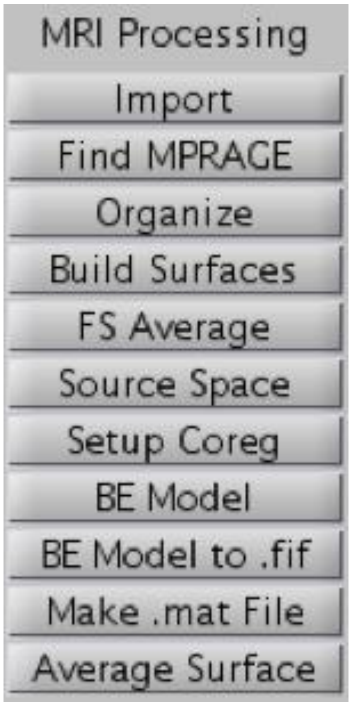


Figure 4.1: MRI Processing Functions

4.1.1 Import

When this program is run, it will ask the user whether to retrieve the raw MRI scan from the Bourget computer cluster or a specified location. If Bourget is selected, it will attempt to find the location of the folder with the subject's MRI on that server using the Martinos command `findsession`. Otherwise, the user can retrieve an MRI scan from a specified folder – most useful when importing from the compact disk drive. On most Linux machines, the CD drive is in the folder `/Media`.

The raw MRI scan will be imported to `<study.mri.rawdir>/<subject.name>`

4.1.2 Finding the T1 MPRAGE file

The next program scans through the subject's raw MRI directory to locate the T1 MPRAGE scan file in order to process the Freesurfer reconstruction. This will use the Martinos center shell command `unpacksdcmdir`. The program scans the unpack.log file for which file corresponds to the entire – or start of – the T1 MPRAGE scan. There may be cases in which this function will not work on the raw MRI data. If the file containing the T1 MPRAGE scan is known, that file can be manually selected using the Structure Editing Interface under the variable `subject.mri.first_mpragefile`.

4.1.3-5 Freesurfer Automatic Reconstruction

The buttons `Organize`, `Build Surfaces`, and `FS Average` are all steps in the Freesurfer reconstruction of the cortical surface. If any of these functions need to be redone, it may be necessary to manually delete the subjects MRI directory in which it writes the file to. The default folder for this is `<study.mri.dir>/<subject.name>`. These programs call on the three primary sections of the recon-all command.

- `Organize` (`-autorecon1`) extracts the important data from the T1 MPRAGE scan
- `Build Surfaces` (`-autorecon2`) creates the white matter, grey matter, scalp, and many other surfaces important for cortical processing
- `FS Average` (`-autorecon3`) maps the subject's brain to the Freesurfer average brain and automatically parcellates the brain into regions.

4.1.6-9 MNE Preparation

The next few buttons call MNE commands in the shell through Matlab.

- `Source Space` (`mne_setup_source_space`) creates a decimated vertex based representation of the cortical surface based on the one made in Freesurfer,. It usually ends up with 10,000 vertices in an effort to compress the data.
- `Setup Coreg` (`mne_setup_mri`) creates the files necessary for the coregistration step found in the MEG routines.
- `BE Model` (`mne_watershed_bem`) constructs the Boundary Element Model used in the source estimation process – particularly for the EEG signals. It also copies a few files to folders for some of the other programs.
- `BE Model to .fif` (`mne_setup_forward_model`) does the steps necessary to set up the forward model.

4.1.10 Converting the surfaces into a Matlab format

In order to decrease the time it takes for the software to load subject's brain data, this function collects all the surfaces and some forward model elements into a Matlab matrix file. When doing this for the last subject, it will automatically attempt to do this for the average subject brain.

4.1.11 Average Brain Surface

This function creates a brain using the Freesurfer command `make_average_subject` to combine the brains of each of the subjects into an average one. Run this command after you have processed the MRIs for all of the subjects in the study.

4.2 Magnetoencephalography

This step prepares the data for the Minimum Norm Estimates analysis, and it requires the most user input.

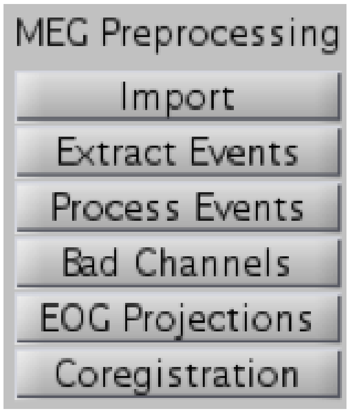


Figure 4.2: MEG Preprocessing Functions

4.2.1 Importing the Scan

After completing the MEG scan that data will be ready to be imported using the `Import` button. The system is configured to first look for the data on the Martinos network `megraid` server. The program will ask for the number of the `megraid` hard drive that the data was saved to and save it to the subject's parameters as `subject.meg.raid`. It will look for the scan data under the folder:

```
 /space/megraid/<subject.meg.raid>/MEG/<study.meg.raid_pi>/subj_<subject.name>
```

If it isn't able to find the right files it will prompt the user to locate the correct directory containing the MEG recordings.

4.2.2&3 Extracting and Processing Events

The Extract Events button will automatically extract the event information to .eve files into the MEG/<subject.name>/triggers directory. Older versions of the MEG software recorded a different event channel so the program will try both channels.

Processing events will require a customized program for each study. It will associate the events recorded during the MEG recording with additional features defined by the user. It will create event files with new event codes based on the primary conditions.

4.2.4 Bad Channels

The user must mark abnormal channels to prevent them from affecting the analysis later on. Channels are usually bad when : 1) There is a large amplitude difference or 2) There is an unusual periodic or random signal not found in other channels. It is often hard to determine exactly if a channel is abnormal. EOG channels should not be marked in this fashion. The user should load one or two blocks in `mne_browse_raw` and write down channels that are abnormal. Then they should click on the button BadChannel and type the identified bad EEG and MEG channels in their respective boxes. These channels will be ignored and not used in the analysis.

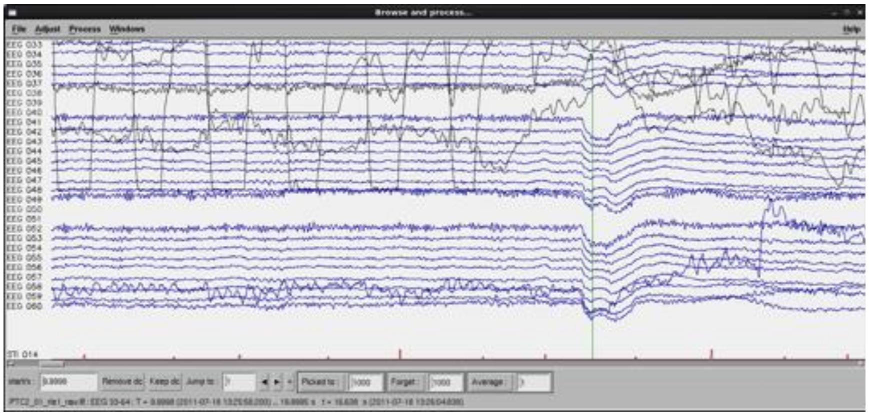
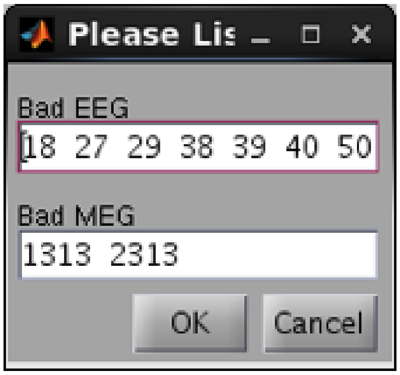


Figure 4.3: mne_browse_raw showing a bad channel in black



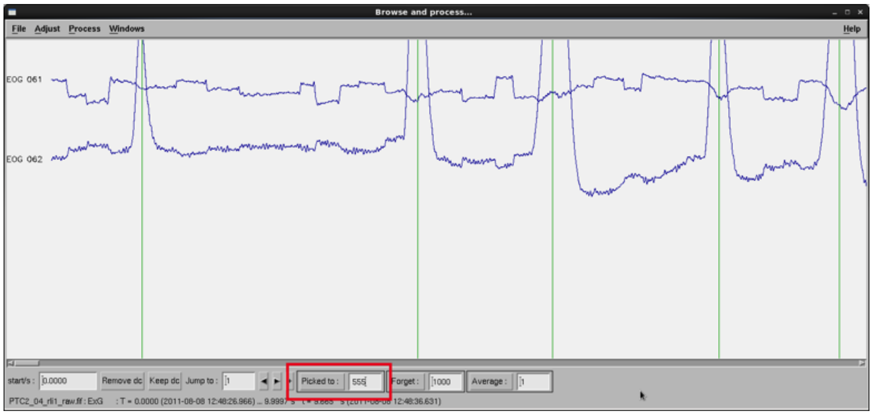
Bad EEG: 18 27 29 38 39 40 50

Bad MEG: 1313 2313

Figure 4.4: The input dialog in GPS: Analysis marking bad channels by channel number designation

4.2.5 Correcting for Blink and Eye Movement Artifacts

Although there are many attested ways to mitigate the effects of eye blinks in brain signals, this software is configured to use the principal component analysis implemented in MNE's `mne_browse_raw` program. In order to use this, the user must open a block of the MEG scan in `mne_browse_raw` and select eye blinks by creating an additional event – conventionally number 555. Scroll through the vertical EOG data and mark the center of the blinks with the cursor then click the "Picked to" button with the number 555. Note the duration of the blink artifacts.



start/s : 0.0000

Jump to : 1

Picked to : 555

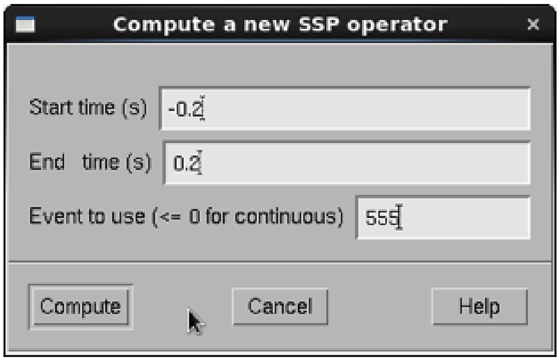
Forget : 1000

Average : 1

PTC2_04_rli1_raw.fif : ExG : T = 0.0000 (2011-08-08 12:48:26.966) ... 9.9997 s (T = 9.665 s (2011-08-08 12:48:36.631)

Figure 4.5: mne_browse_raw showing the EOG channels with marked artefacts

Click on the function `Process/Create a new SSP Operator…`. This command performs a principal component analysis of the data, based on the time period selected. We will use this analysis to identify the principal components related to blinking. The routine allows the user to enter the start time and the end time of the subject’s blinks relative to the marks created for the particular event number. For instance, in the data shown (see figure 4.6) the blinks are 400 ms long and marked to the channel 555. If this process fails, it is likely because it was not able to locate enough time samples in this window, so more blinks should be selected or there could be another issue with the data.



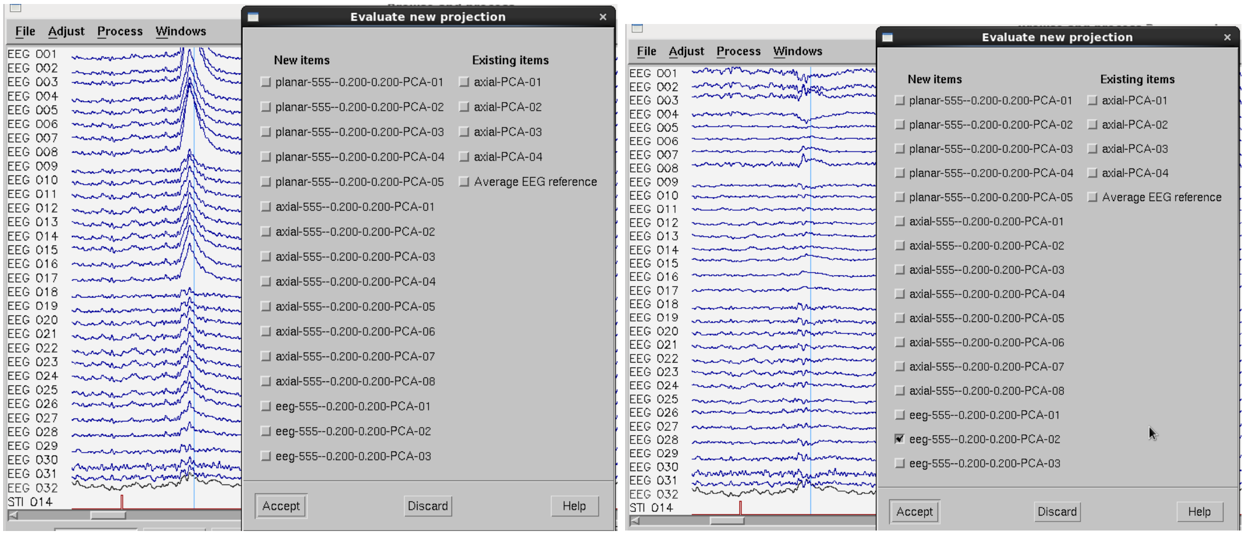
Start time (s) -0.2

End time (s) 0.2

Event to use (<= 0 for continuous) 555

Figure 4.6: Dialogue in mne_browse_raw prompting the user to select a time window

Now, a menu of principal component analysis projections will appear. Multiplying the data by these projections (vectors) should remove artifacts from the raw data. PCA decomposes components that reflect the major underlying signals. The most prominent components will be the blinks, but be very careful: auditory processing signals may also be detected by the data; if they are screened out using the principal component analysis then the data is destroyed. Thereby, the task is to identify the components that affect the data the most negatively and are correlated with the eye blinks. The saved eye blink events will have light blue lines so the events can be seen on the EEG and MEG channels. Select projections for the EEG channels, the MEG planar gradiometers, and the MEG axial magnetometers. It is useful to find a page of channels that are overtly influenced by the blinks to operate on.



Evaluate new projection

New items
- ☐ planar-555--0.200-0.200-PCA-01
- ☐ planar-555--0.200-0.200-PCA-02
- ☐ planar-555--0.200-0.200-PCA-03
- ☐ planar-555--0.200-0.200-PCA-04
- ☐ planar-555--0.200-0.200-PCA-05
- ☐ axial-555--0.200-0.200-PCA-01
- ☐ axial-555--0.200-0.200-PCA-02
- ☐ axial-555--0.200-0.200-PCA-03
- ☐ axial-555--0.200-0.200-PCA-04
- ☐ axial-555--0.200-0.200-PCA-05
- ☐ axial-555--0.200-0.200-PCA-06
- ☐ axial-555--0.200-0.200-PCA-07
- ☐ axial-555--0.200-0.200-PCA-08
- ☐ eeg-555--0.200-0.200-PCA-01
- ☐ eeg-555--0.200-0.200-PCA-02
- ☐ eeg-555--0.200-0.200-PCA-03

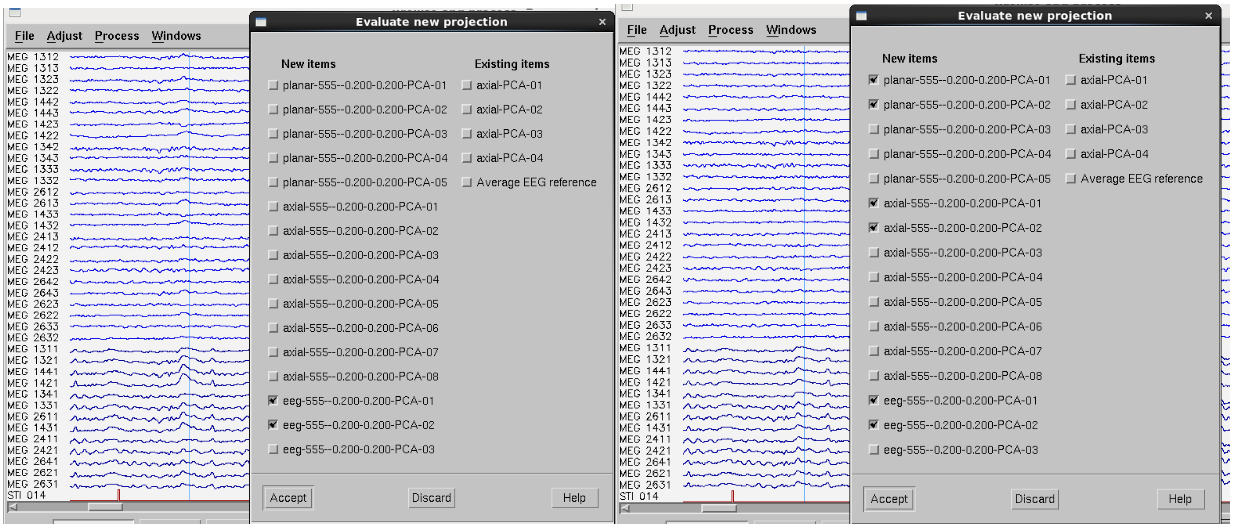
Existing items
- ☐ axial-PCA-01
- ☐ axial-PCA-02
- ☐ axial-PCA-03
- ☐ axial-PCA-04
- ☐ Average EEG reference

Evaluate new projection

New items
- ☐ planar-555--0.200-0.200-PCA-01
- ☐ planar-555--0.200-0.200-PCA-02
- ☐ planar-555--0.200-0.200-PCA-03
- ☐ planar-555--0.200-0.200-PCA-04
- ☐ planar-555--0.200-0.200-PCA-05
- ☐ axial-555--0.200-0.200-PCA-01
- ☐ axial-555--0.200-0.200-PCA-02
- ☐ axial-555--0.200-0.200-PCA-03
- ☐ axial-555--0.200-0.200-PCA-04
- ☐ axial-555--0.200-0.200-PCA-05
- ☐ axial-555--0.200-0.200-PCA-06
- ☐ axial-555--0.200-0.200-PCA-07
- ☐ axial-555--0.200-0.200-PCA-08
- ☐ eeg-555--0.200-0.200-PCA-01
- ☑ eeg-555--0.200-0.200-PCA-02
- ☐ eeg-555--0.200-0.200-PCA-03

Existing items
- ☐ axial-PCA-01
- ☐ axial-PCA-02
- ☐ axial-PCA-03
- ☐ axial-PCA-04
- ☐ Average EEG reference

Figure 4.7: EEG channels with a blink before and after a successful projection



Evaluate new projection

New items
- ☐ planar-555--0.200-0.200-PCA-01
- ☐ planar-555--0.200-0.200-PCA-02
- ☐ planar-555--0.200-0.200-PCA-03
- ☐ planar-555--0.200-0.200-PCA-04
- ☐ planar-555--0.200-0.200-PCA-05
- ☐ axial-555--0.200-0.200-PCA-01
- ☐ axial-555--0.200-0.200-PCA-02
- ☐ axial-555--0.200-0.200-PCA-03
- ☐ axial-555--0.200-0.200-PCA-04
- ☐ axial-555--0.200-0.200-PCA-05
- ☐ axial-555--0.200-0.200-PCA-06
- ☐ axial-555--0.200-0.200-PCA-07
- ☐ axial-555--0.200-0.200-PCA-08
- ☑ eeg-555--0.200-0.200-PCA-01
- ☑ eeg-555--0.200-0.200-PCA-02
- ☐ eeg-555--0.200-0.200-PCA-03

Existing items
- ☐ axial-PCA-01
- ☐ axial-PCA-02
- ☐ axial-PCA-03
- ☐ axial-PCA-04
- ☐ Average EEG reference

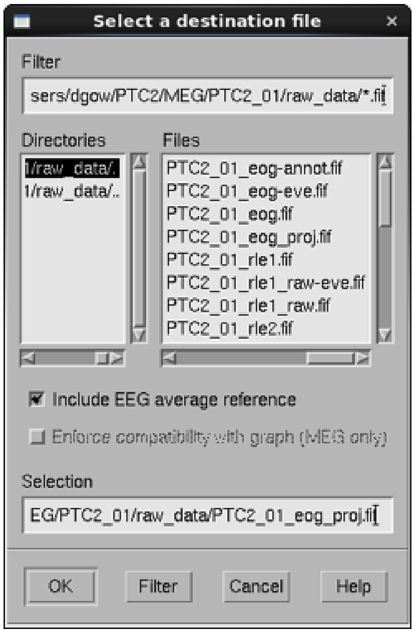
Evaluate new projection

New items
- ☑ planar-555--0.200-0.200-PCA-01
- ☑ planar-555--0.200-0.200-PCA-02
- ☐ planar-555--0.200-0.200-PCA-03
- ☐ planar-555--0.200-0.200-PCA-04
- ☐ planar-555--0.200-0.200-PCA-05
- ☑ axial-555--0.200-0.200-PCA-01
- ☑ axial-555--0.200-0.200-PCA-02
- ☐ axial-555--0.200-0.200-PCA-03
- ☐ axial-555--0.200-0.200-PCA-04
- ☐ axial-555--0.200-0.200-PCA-05
- ☐ axial-555--0.200-0.200-PCA-06
- ☐ axial-555--0.200-0.200-PCA-07
- ☐ axial-555--0.200-0.200-PCA-08
- ☑ eeg-555--0.200-0.200-PCA-01
- ☑ eeg-555--0.200-0.200-PCA-02
- ☐ eeg-555--0.200-0.200-PCA-03

Existing items
- ☐ axial-PCA-01
- ☐ axial-PCA-02
- ☐ axial-PCA-03
- ☐ axial-PCA-04
- ☐ Average EEG reference

Figure 4.8: MEG channels with a blink before and after a successful projection. Note that the non-blink related bump a few hundred milliseconds after the blink is preserved.

Once the projections that clean up the blinks have been selected, select all the existing projections. Before you save, make sure that the "Include EEG average reference" option has been checked. Click accept and save the file as `<subject.name>_eog_proj.fif` in the subject's MEG raw data directory. As long as the analysis interface shows that you have the same eog projection file it will automatically apply the EOG projections.



Filter

sers/dgow/PTC2/MEG/PTC2_01/raw_data/*.fif

Directories

1/raw_data/.
1/raw_data/..

Files

PTC2_01_eog-annot.fif
PTC2_01_eog-eve.fif
PTC2_01_eog.fif
PTC2_01_eog_proj.fif
PTC2_01_rle1.fif
PTC2_01_rle1_raw-eve.fif
PTC2_01_rle1_raw.fif
PTC2_01_rle2.fif

☑ Include EEG average reference

☐ Enforce compatibility with graph (MEG only)

Selection

EG/PTC2_01/raw_data/PTC2_01_eog_proj.fif

Figure 4.9 mne_browse_raw projection saving prompt

4.2.6 Coregistration

The next step is to align the location of the head in the MEG experiment to the MRI reconstruction. To perform this, open the MNE program `mne_analyze` – found under the utility stage. This can only be done after the MRI and MEG have been processed. Note that this is part of the usual MNE MEG/EEG analysis and is not specific to GPS.

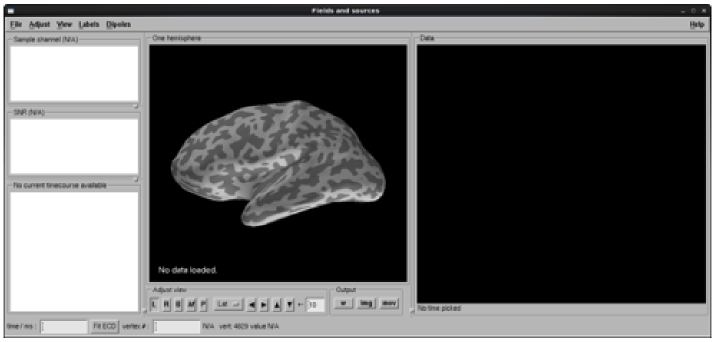
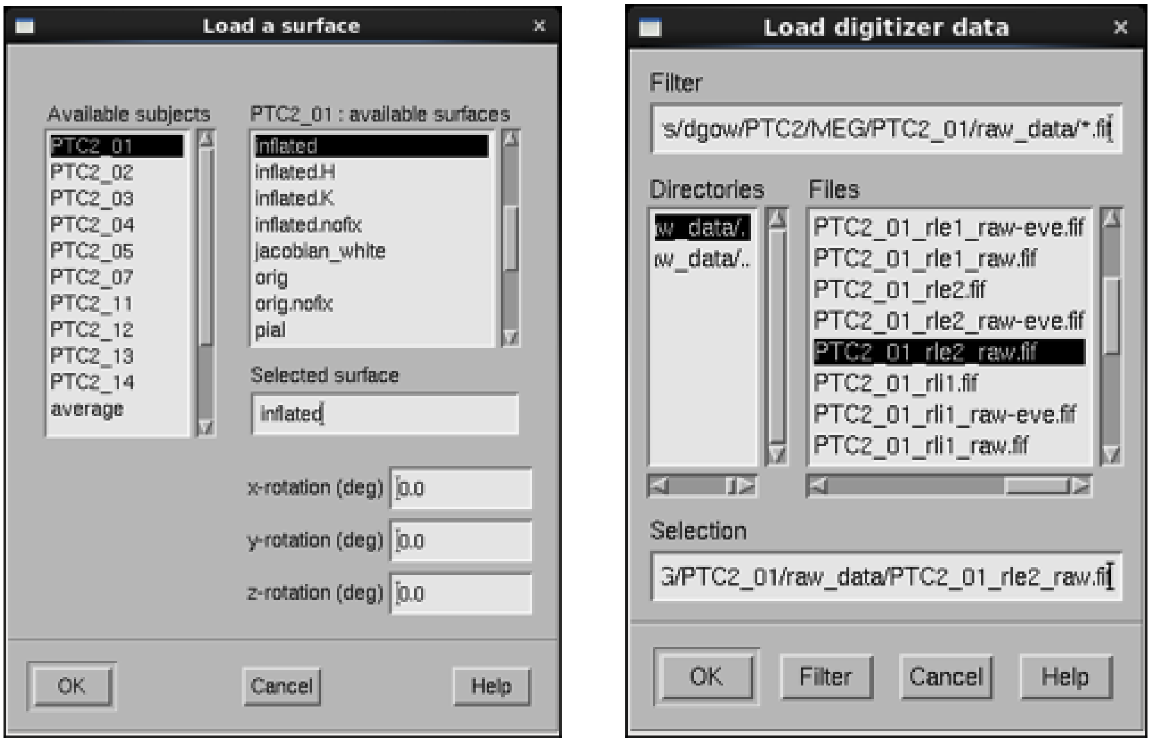


Figure 4.10 mne_analyze cold open with a subject loaded

This interface is largely used to open the MNE maps after the inverse model is created. For the purposes of coregistration, just load the surface and the digitization data. Any surface for the subject will work well for this task. The digitization data is found in the raw MEG data files. Coregistration happens only once, so pick the block in which the subject's head is approximately in the middle of all of the blocks – mitigating head movement misalignment.



Selected surface: inflated

x-rotation (deg): 0.0

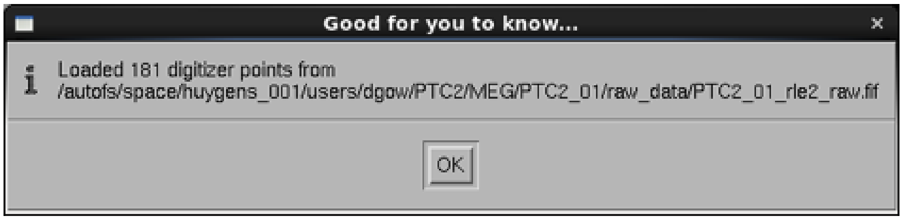
y-rotation (deg): 0.0

z-rotation (deg): 0.0

Filter: s/dgow/PTC2/MEG/PTC2_01/raw_data/*.fif

Selection: G/PTC2_01/raw_data/PTC2_01_rle2_raw.fif

Figure 4.11 menus to select a surface and menu to load digitizer data.



Loaded 181 digitizer points from
/autofs/space/huygens_001/users/dgow/PTC2/MEG/PTC2_01/raw_data/PTC2_01_rle2_raw.fif

Figure 4.12 Information presented when a subject is correctly loaded.

Next, open the head viewer under `Viewer/Show viewer…` Change the options to not show the cortex, transparent scalp, and show digitizer data.

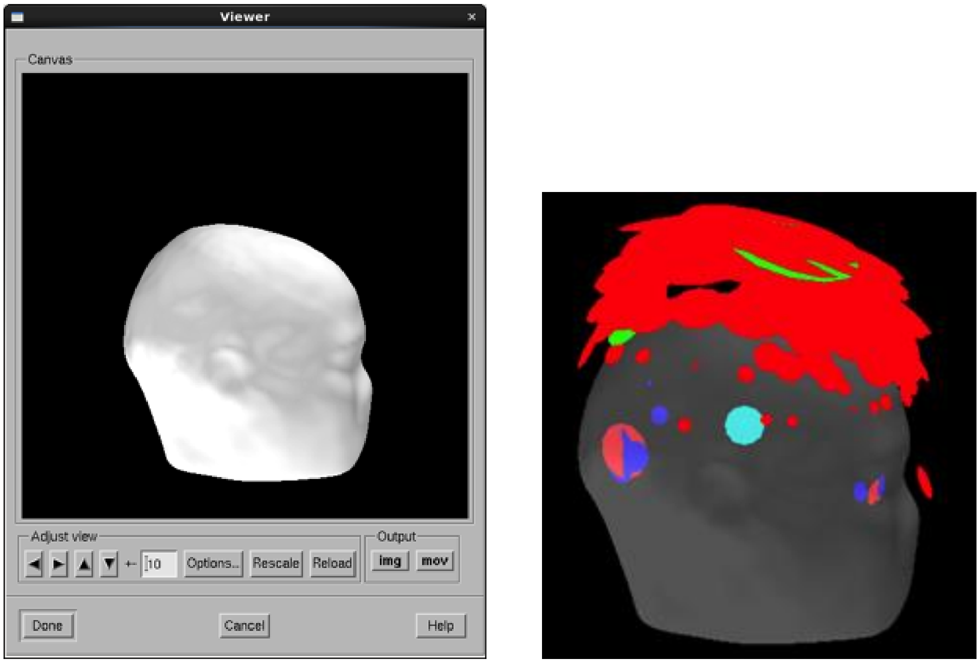
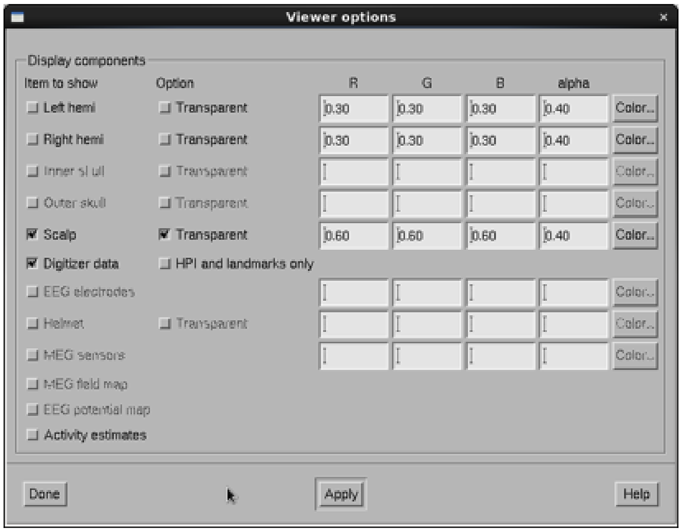


Figure 4.13 MRI head surface viewer at load and after selecting the head coordinates

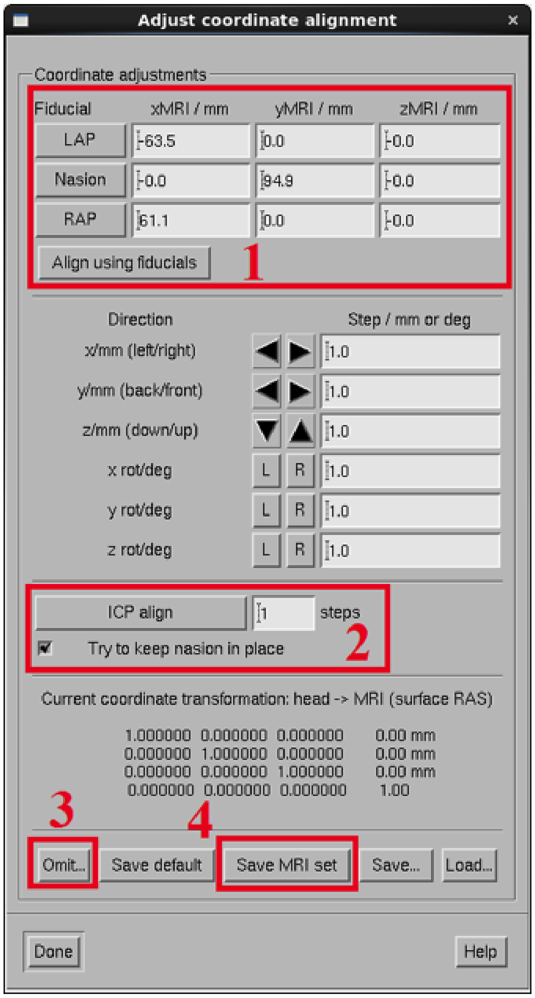


Display components

Item to show	Option	R	G	B	alpha	
☐ Left hemi	☐ Transparent	0.30	0.30	0.30	0.40	Color...
☐ Right hemi	☐ Transparent	0.30	0.30	0.30	0.40	Color...
☐ Inner skull	☐ Transparent					Color...
☐ Outer skull	☐ Transparent					Color...
☒ Scalp	☒ Transparent	0.60	0.60	0.60	0.40	Color...
☒ Digitizer data	☐ HPI and landmarks only					
☐ EEG electrodes						Color...
☐ Helmet	☐ Transparent					Color...
☐ MEG sensors						Color...
☐ MEG field map						
☐ EEG potential map						
☐ Activity estimates						

Figure 4.14 Viewer options to visualize head coordinates

Now, open the `Coordinate alignment` interface under the `Adjust` menu. The first task will be to select the locations of the fiducials on the scalp. For each point, click each fiducial button (`LAP` – Left Auricular Point, `Nasion`, `RAP`) in Figure 4.15 area 1, and then click the approximate corresponding location for each point on the scalp.



Adjust coordinate alignment

Coordinate adjustments

Fiducial	xMRI / mm	yMRI / mm	zMRI / mm
LAP	-63.5	0.0	-0.0
Nasion	-0.0	94.9	-0.0
RAP	61.1	0.0	-0.0

Direction		Step / mm or deg
x/mm (left/right)	◀ ▶	1.0
y/mm (back/front)	◀ ▶	1.0
z/mm (down/up)	▼ ▲	1.0
x rot/deg	L R	1.0
y rot/deg	L R	1.0
z rot/deg	L R	1.0

ICP align 1 steps

☑ Try to keep nasion in place

Current coordinate transformation: head -> MRI (surface RAS)

```
1.000000  0.000000  0.000000     0.00 mm
0.000000  1.000000  0.000000     0.00 mm
0.000000  0.000000  1.000000     0.00 mm
0.000000  0.000000  0.000000     1.00
```

Figure 4.15 Coordinate alignment menu

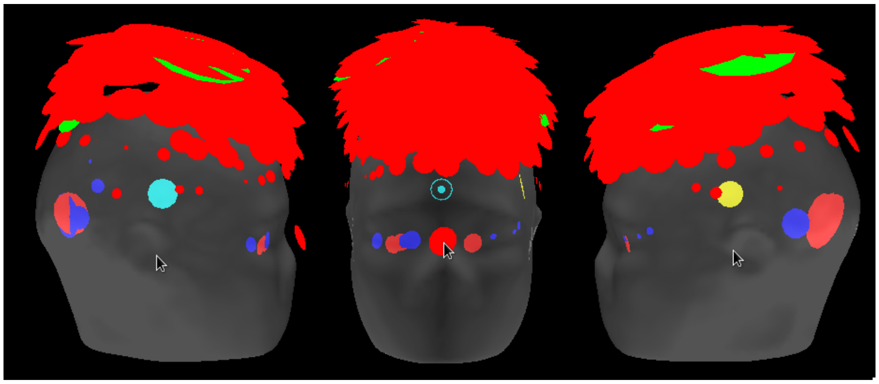


Figure 4.16 Subject’s scalp surface with mouse cursor above the three fiducials, from left to right: RAP, Nasion, LAP

After the fiducials have been located, click `Align using fiducials` and it will align the EEG points to the scalp. Each circle corresponds to each point clicked on by the digitizing pen. The size of the circles reflects the distance from the MRI computed scalp. Blue circles represent points inside the scalp and red circles represent points outside the scalp.

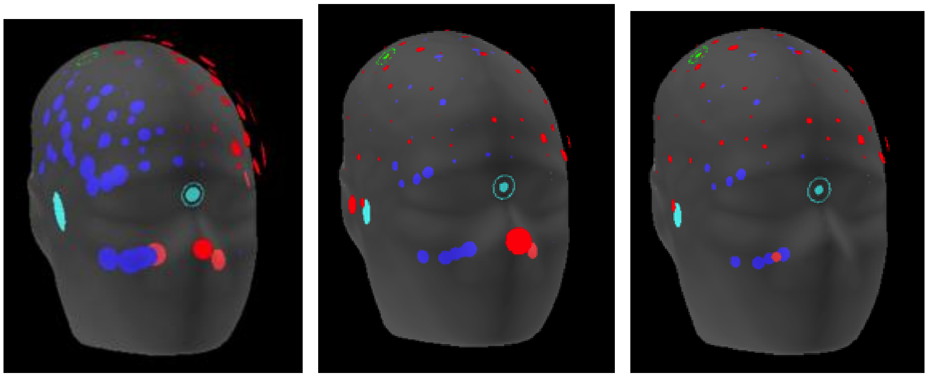
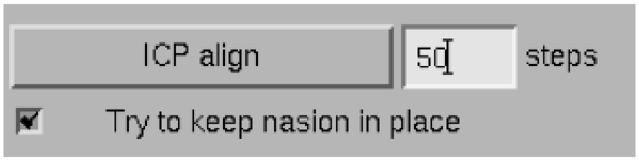


Figure 4.17 Scalp surface in in three stages

1) After fiducial alignment
2) After automated ICP alignment
3) After discarding far points and additional ICP alignment

In order to refine the alignment, let the program automatically align the points to the best fit. Under the `ICP align` option in area 2 (and see in figure 4.18), set it to 50 steps and click the button. This will move the points to a better fit to the scalp.

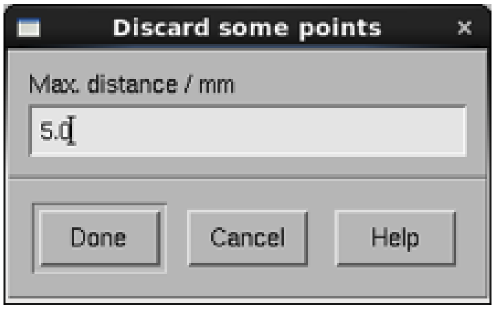


50 steps

☑ Try to keep nasion in place

Figure 4.18 Automatic alignment box

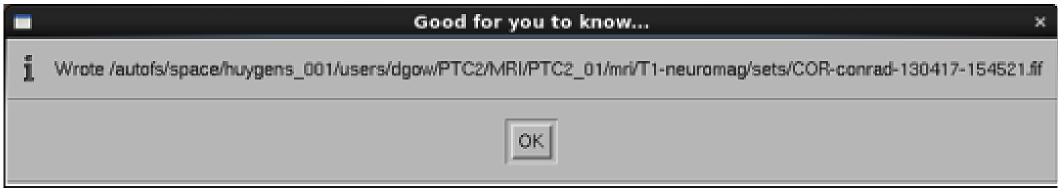
Next, discard the points that are far away and are biasing the automatic alignment by omitting points that are more than half a centimeter away. This button is found in area 3 of the coordinate alignment interface. Then click the `ICP align` button again.



Max. distance / mm: 5.0

Figure 4.19 Point discard selection box

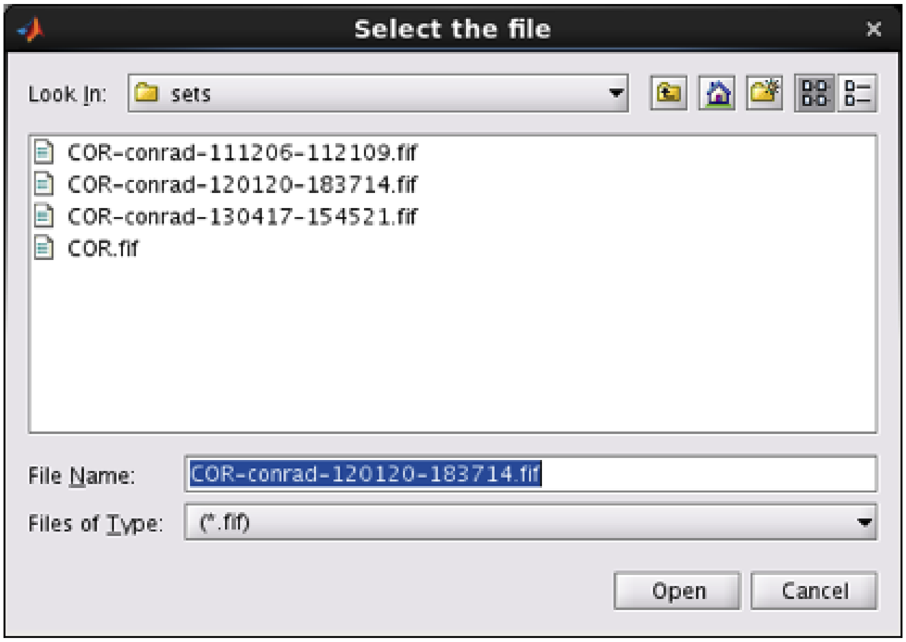
Save the coregistration using the `Save MRI set` button in area 4. It will save a file in the subject's MRI directory with the date and time of this coregistration.



Wrote /autofs/space/huygens_001/users/dgow/PTC2/MRI/PTC2_01/mri/T1-neuromag/sets/COR-conrad-130417-154521.fif

Figure 4.20 Saving dialog

Back in the Analysis interface, click on the `MEG/Coregistration` button and select the file that was just created in the `mne_analyze` interface.



COR-conrad-111206-112109.fif
COR-conrad-120120-183714.fif
COR-conrad-130417-154521.fif
COR.fif

File Name: COR-conrad-120120-183714.fif
Files of Type: (*.fif)

Figure 4.21 Selecting that saved file in the GPS Analysis prompt

4.3 Minimum Norm Estimates

This stage of the analysis constructs a matrix that maps sensor activity to the cortical surface. Each function is highly automated, therefore user should only split it into phases in case certain stages need to be re-run.

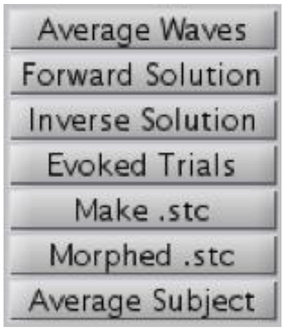


Figure 4.21 MNE Processing Functions

4.3.1 Averaging Sensor Data

After the events have been processed, bad channels marked, and EOG projection made, the data from the sensors can be averaged. Averaging the MEG and EEG waves will increase the signal to noise ratio. This step will create `.fif` files containing the waves. It will first make files for each block and then an average for the whole subject. This stage will also create averages for the covariance processing in order to weigh down noisy channel data. It is important to be familiar with the `study.mne` parameters and the `condition.event` parameters. Before processing this, consult Appendix 2. This step will only create averages for conditions considered primary conditions. This process filters out frequencies higher than 60 Hz from the sensor data. Filtered block `.fif` files are saved in `<subject.meg.dir>/processed_data/` and are used later in the Granger analysis.

4.3.2&3 MNE Forward and Inverse Solution

These programs route information to the MNE routines that create a model mapping cortical activity to sensor activity and then back around. There are particular options that can be changed for this process if the Matlab code is modified.

4.3.4 Extract Evoked Trials

The next step is to gather the evoked trials into groups based on each event code set in the Process Events step. It will make a series of .mat files with names based on the event codes that can be collected later on for trial analysis.

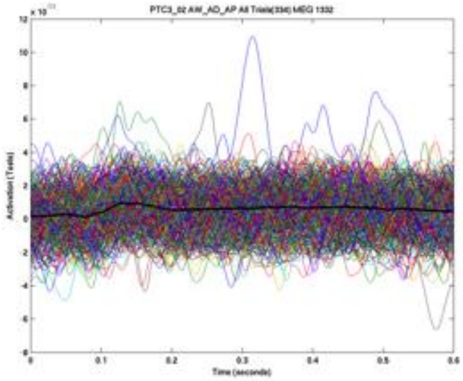


Figure 4.22 Figure generated in extracting evoked trials showing the mean. Please be careful of the high variance natural in EEG data.

4.3.5-7 Source Timecourses and Average Cortex Maps

These functions make source timecourses, illustrating the activity on the cortical surface over time. The `Make .stc` function creates stc files with the mne tag based on the sensor averages and the inverse solution – only for the primary conditions. The `Morphed .stc` function will make stc files on the average cortical surface It is done in the same manner as the primary conditions, but it will also convert act tagged .stc files for secondary conditions made during the `granger->condition` phase. The `Average Subject` button will combine the morphed .stc files.

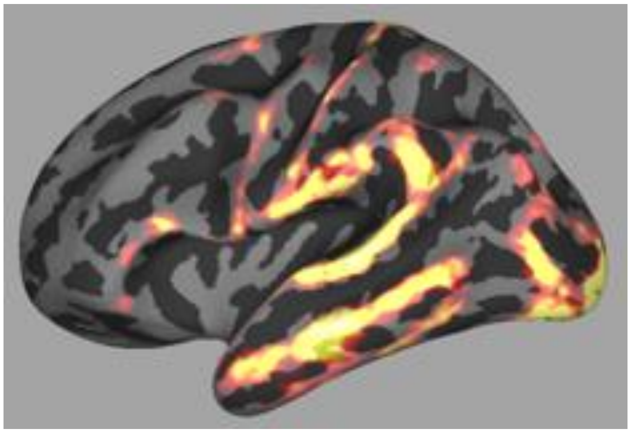


Figure 4.23 Neural activation computed by MNE projected on the brain

4.4 Phase Locking Values

Please note that this function has been temporarily removed from the interface and will be restored later when the group is satisfied with it. To restore the PLV stage, manually edit the gps_presets.m file and add a stage called "plv" to the stages and stage_names fields. Additional stages can also be added by editing this part. You will need to edit gpsa_load_stage.m for additional stages

In order to better locate regions of interest, our lab sought to make use of metrics related to functional connectivity. Phase locking values measure the similarity in the phase of two waves. The technique takes a label for one region of interest and computes the phase locking between that area and the rest of the brain, generating `.stc` files similar to the ones in the MNE stage.

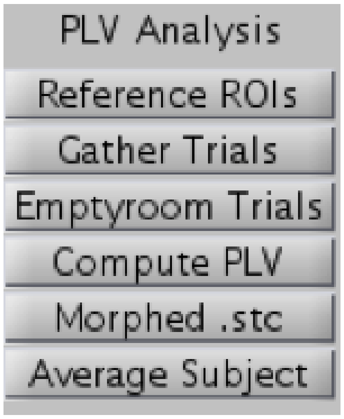


Figure 4.24 PLV Analysis functions

4.4.1 Region of Interest

The program expects the user to create a region of interest `.label` file (either in `mne_analyze` or in the ROI interface) and put it in the `<study.plv.dir>/rois/<condition.name>` folder. The Reference ROIs button will map average subject labels to each individual subject. If multiple labels are in that folder they will also be mapped, but usually only one reference ROI will be used in the PLV analysis. The program will also create an image of the reference vertex on the brain showing were the vertices were located with the cortical activation backdrop.

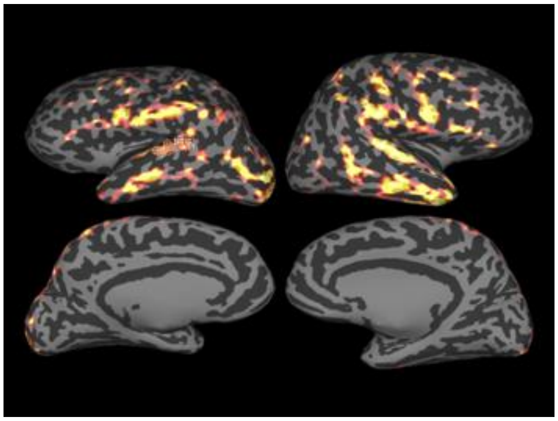


Figure 4.25 Neural Activation looked at to make a reference ROI

4.4.2 & 3 Acquiring Trial Data for PLV Analysis

The next two buttons extract sensor data and put them into `.mat` files to be used in the `Compute PLV` routine. `Gather Trials` gets evoked responses from the `condition.event` parameters. `Emptyroom Trials` extracts chunks of time for simulated trials from the subjects emptyroom file.

4.4.4 Computing Phase Locking

Functional connectivity analyses provide an obvious tool for identifying ROIs. We are extremely interested in the use of ~40 Hz gamma phase locking meaures for this purpose. In theory, one would identify a reference ROI and identify other ROIs based on phase locking with this signal. This routine will generate `.mat` and `.stc` movies of the phase locking values on the subject's cortical surface. However**, we caution against using them in their current form** because these analyses show a strong spatial bias to the region around the reference site.

4.4.5-6 Average Brain Timecourses

For group level analysis, the `Morphed .stc` button maps the subject's phase locking `.stc` file to the average brain. `Average Subject` will combine the morphed files to get a study-wide average of phase locking.

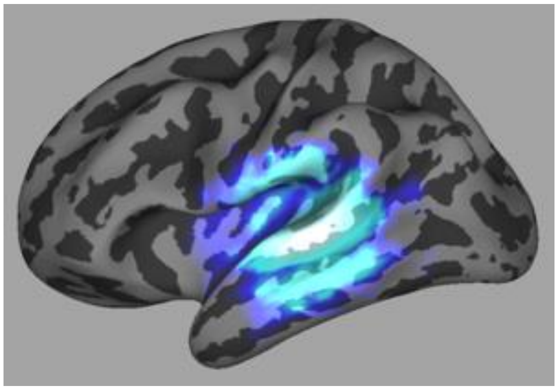


Figure 4.26 Phase locking values to the STG mapped on to the cortex

4.5 Granger Causality

The final stage of the MEG analysis is to compute the functional connectivity measured in Granger causality created using Kalman filters.

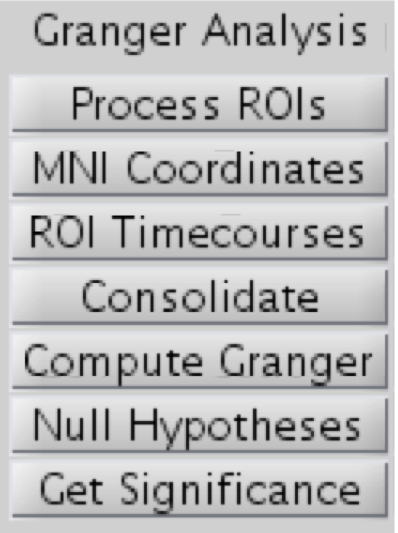


Figure 4.24 Granger analysis functions

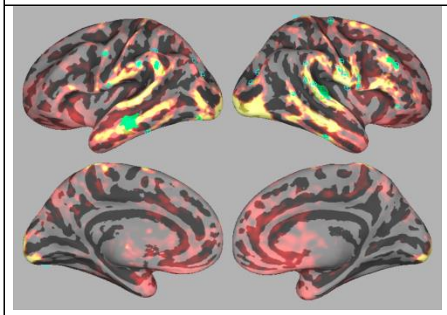
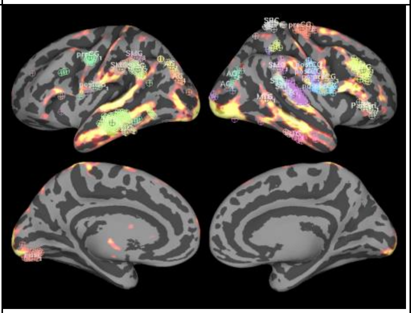
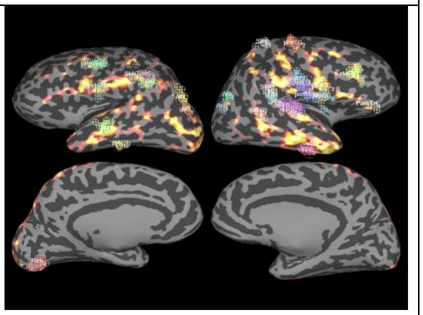
4.5.1&2 Regions of Interest

To begin Granger analysis, first define a set of regions of interest to be used in the granger analysis. This step must be done with great care because it influences the strength of inferences that can be made, the sensitivity of the measures, and the processing demands of the analyses. Using too few ROIs may increase the likelihood of spurious correlation. One should make every effort to include all plausibly interacting ROIs in a system. Using ROIs with timecourses that are too similar reduces the sensitivity of Granger analyses. When creating ROIs one must therefore respect the limits of the imaging modalities spatial resolution. Using too many ROIs may also make analyses computationally unwieldy. This is in many ways an exercise in constraint satisfaction. In our experience, we tend to get the best results when using 15-50 ROIs, each consisting of 100-1000 full brain vertices or -50 MNE decimated brain vertices. This of course is a function of the task and the spatial resolution of the source reconstruction.

The Region of Interest interface can be used to make the set of cortical labels and is integrated into the stream. Otherwise, for each condition, put the condition’s MNE `.label` files in the `<study.granger.dir>/rois/<condition.granger.roiset>` directory. Multiple conditions can share the same ROI set, in fact that is advised for comparable analysis later on. For single subject analysis, put the label files in that directory in a subfolder of the subject’s name.

Running the `Process ROIs` button will make `.mat` files from the labels. If the ROIs were made on the average cortical surface, it will spin them back to the subjects. Regardless, for each subject/condition pair this is run on, the routine will locate the vertices with the highest cortical activation within each region. These vertices are used to get the activation profiles to be used in the Granger computation. Some later programs will want the average subject’s vertices.

The `MNI Coordinates` button will retrieve the MNI coordinates of the region's central vertices for reporting.

ROIs generated in the ROI interface. `GPSr.m`	ROIs interpreted for average brain vertices in `gpsa_granger_rois.m`	ROIs spun back to a subject using `gpsa_granger_rois.m`
		

4.5.3&4 Gather Timecourses

The next step is to gather data for each subject (or group of trials) for each wave going into the Kalman filter.

1. `ROI Timecourses`: Get the ROI profiles for each condition based on the processed ROI centroids made in `Process ROIs` and the activation `.stc` files made in the `MNE/Evoked Trials`. Single subject studies will average groups of trials and give multiple waveforms for each subject.
2. `Consolidate`: Collect timecourses for each subject or set into a single input file for the Granger/Kalman filters. This will also interpolate all timecourses to 1000 Hz so that Granger data can be studied directly at the millisecond resolution.

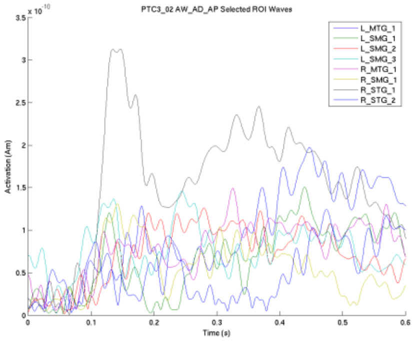


Figure 4.26 Automatically generated graph showing the timecourses for multiple ROIs.

4.5.6 Computing Granger-Causality using Kalman Filters

Before executing this function, make sure the parameters are set according to your design. The two most important parameters are `study.granger.model_order` and `study.granger.W_gain`. The model order refers to the number of time lags used in the Kalman filter to predict future epochs. A model order of 7, for instance, will use the data of the past 7 samples, incidentally the past 7 ms, to predict each future time point. This number can be computed empirically using Bayesian Information Criteria or another method, but this is not currently built into the GUI.

The `W_gain` variable refers to the prediction adaptation, the amount that the prediction matrix changes in each round relative to the prediction error. A `W_gain` of 0.5 will half the influence of the past computation so the model will change dynamically. A `W_gain` of 0.03 will be more conservative.

Pressing `Compute Granger` will run `gps_granger` and `gps_kalman` in order to determine functional connectivity. This function will process the vertices but it will not produce any visuals, use the plotting GUI for that purpose. Functional connectivity is computed by creating time varying autoregressive models based on the signal data of the ROIs as selected above. This routine will create a Kalman filter with the full set of ROIs and once for each ROI -- running the full set minus the selected ROI. If the prediction error of the Kalman filter is increased by losing an ROI, it is inferred that the inclusion of the ROI was helpful for prediction and thereby Granger-causes another. The results are called Granger causality indices.

4.5.7 Generating Null Hypotheses to measure significance

The Granger results, although clear time courses, do not necessarily establish significant Granger-causality. Each model has factors based on the number of ROIs and underlying neural processes. In order to establish which periods of Granger-causality are significant, the model is run numerous times with small perturbations that should remove causality. Usually, we produce this modified model 2000 times, this parameter can be modified at `study.granger.N_comp`. This will create a very large matrix with the Granger causality indices for 2000 models, between each ROI, for each timepoint. The size of this matrix could easily be 500MB and it could take hours or days to compute (even though it uses parallel processing) , thus it is advised that users only do this operation when satisfied with the data.

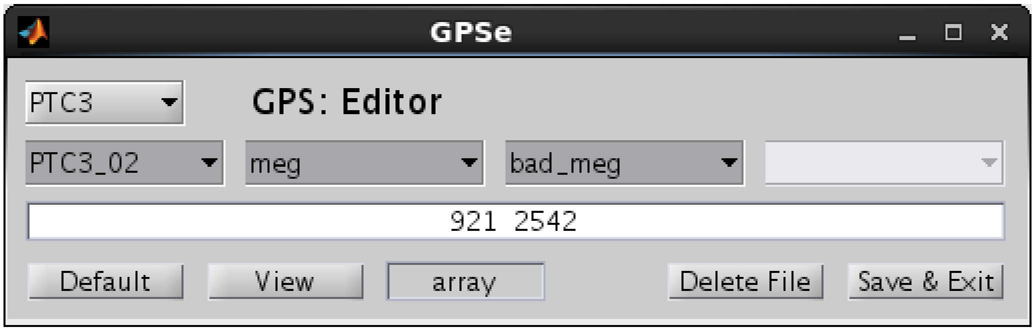
The original data are altered by taking the original Kalman filter and reconstructing the data. For each pair of regions A and B, the coefficients of the prediction matrix (also called the state process), mapping A to B are zeroed out and the residuals are shuffled so it produced a slightly noisier version of the original regions' signals without the predicted connection. Under this restriction, if region A still has high Granger causality index (GCI) in causing B, then the original index is less significant.

4.5.8 Get Significance

This last function loads in the null hypothesis file and generates some inferential statistics based on it (such as p values). It saves this analysis in the results folder. After this step is done, you can see your data in the GPS: Plot Drawer, as explained in Chapter 7.

Chapter 5: Structure Editing Interface

This interface assists the user in editing parameters for each study. A description of each parameter is in Appendix 2.



Selection

There are five drop-down lists. The list on the left-top corner changes which study folder is being viewed. The list below that, the leftmost list in the middle row, controls which file is opened. Most of these files will be the study parameter, with just the name of the study,subjects or conditions. There may be extra files listed that are `.mat` files in the study's parameter directory that the interface does not recognize and thereby cannot change.

The next three dropdown lists specify fields within the parameter file. Fields that are substructures are expanded into the next list. For instance, shown on the screen is the parameter `subject.meg.bad_meg` which recalls the numbers of the bad MEG channels. Changing files will not alter the substructure configuration that is open, making it easier to change parameters systemically between sets.

Options

The white bar in the middle can be used to edit most fields. The data type expected for each field is listed in the middle-bottom box

The delete file key has not been enabled yet.

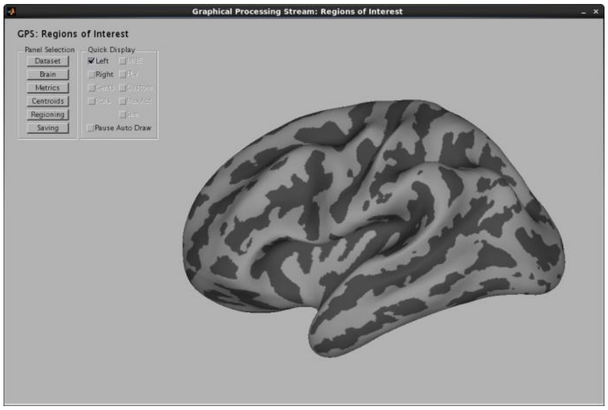
Saving

Parameters are saved after changing files (subjects, conditions…) and by pressing the `Save & Exit` button.

Chapter 6: Region of Interest Interface

Cortical activity reconstructions generate data for thousands or tens of thousands of locations across the brain, (vertices in the 2D grey matter surface for MNE). Most algorithms and group level analysis are performed over vertices in an averaged cortical surface.

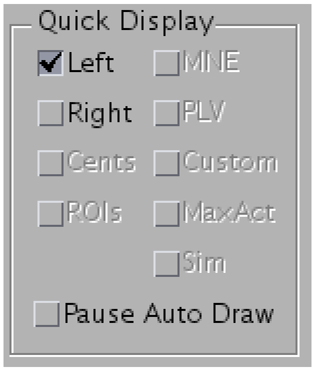
A GUI was constructed to automate and facilitate the creation of ROIs. Our create a reliable, transparent and objective process for identifying ROIs that meet the assumptions of Granger analysis. The next pages describe how functions are organized within each menu of this GUI, followed by an outline showing the process used to create regions of interest



Organization

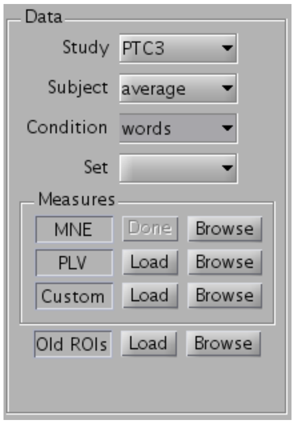
The graphical user interface has panels on the left hand side and image(s) of the brain on the right. Over time the program will generate additional figures showing activation profiles, similarity matching, and region forming. When the program is booted, it will open a figure that retains activation movies and other heavy data in memory – do not close this figure as it is necessary to keep the information without slowing the program down.

There is also a menu used to quickly toggle visualization options. As data is loaded, these options are unlocked. The options `Left` and `Right` select whether or not to show those hemispheres. `Cents` allows visualization of centroid vertices. `ROIs` displays regions of interest across the cortical surface. `Pause Auto Draw` will pause the automatic generation of new brain images in case many options are being changed – otherwise with every edit the surface is redrawn, which could contribute to long loading times. The other five options toggle whether each metric's information is shown on the cortical surface.



Loading Data

By clicking on the Dataset button in the panel list, a new panel is opened to select data to load. There are four drop down lists that allows the selection of the study, subject, condition, and set (defunct). These options are loaded from what is provided in the



Study PTC3

Subject average

Condition words

analysis GUI and call their parameters from the same parameter files as the rest of the study. The set list corresponds to a dated feature to select multiple sets of regions for the same condition. Ideally, each condition will be different. The program will automatically retrieve the necessary brain information for the subject selected.

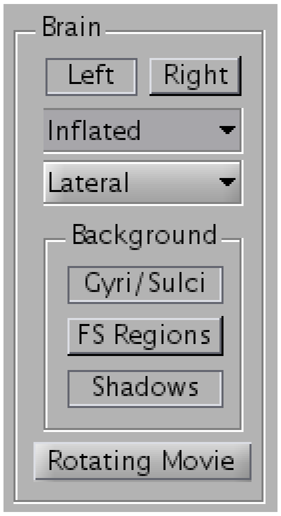
The Measures list allows `.stc` and certain .mat files to be loaded into the program. It will automatically expect certain file names based on what the analysis program's default are. The browse button will allow the user to select different `stc` or mat files. When selecting an `stc` file, select the left hemisphere one and it will automatically find the right hemisphere based on the filename.

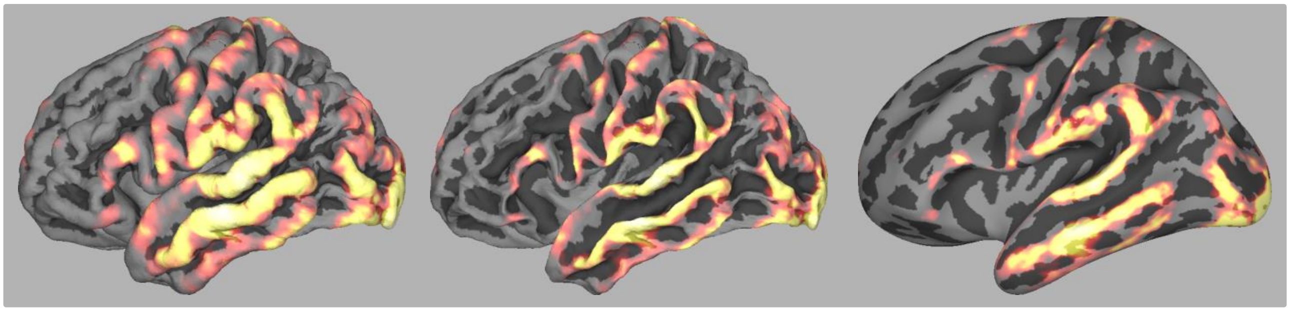
Brain Viewing Options

The brain panel shows options for the cortical surface visualization. The `Left` and `Right` buttons are used to select which hemispheres will be displayed. The `Rotating Movie` button will create a movie of the brain rotating with whatever settings are currently enabled. This function is optional, and may not support all types of data.

Surface

This dropdown list will enable the user to change which cortical representation is shown. Each surface is loaded from the Freesurfer reconstruction.

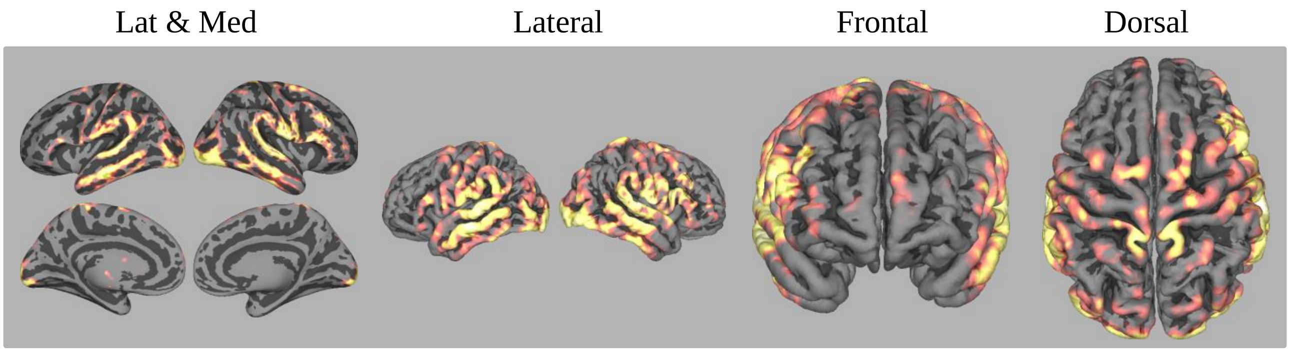




Pial (Grey Matter) White Matter Inflated

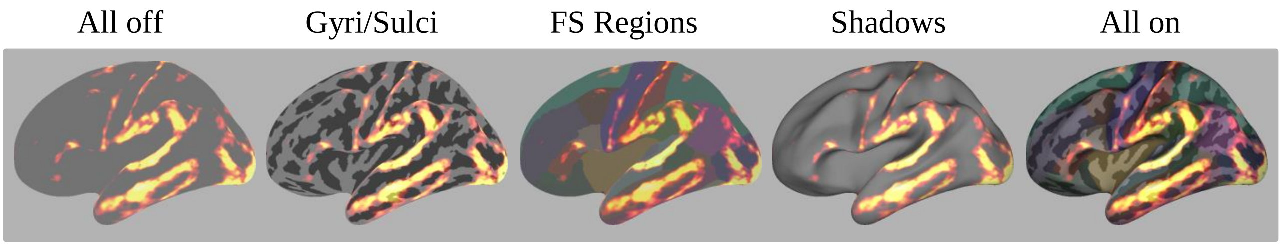
Viewing Angle

The viewing angle can also be adjusted. The 6 cubic views are options in the drop down – `Lateral`, `Medial`, `Frontal`, `Occipital`, `Dorsal`, and `Ventral`. There are two more views. The first is `Lat & Med` which loads both the lateral and medial surfaces –showing the lateral on top. The last view option `Free Rotate` unlocks the free rotation option for Matlab figures. It gives the cursor the ability to drag and move to parts of the brain.



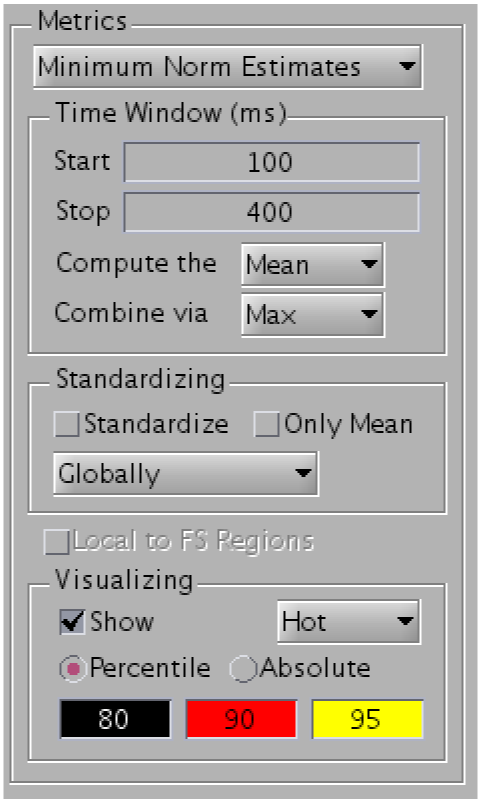
Background Overlays

There are many useful overlays available to make cortical features more visible. The information used to build the overlays also comes from the Freesurfer reconstruction. The `Gyri/Sulci` overlay will color gyri in light grey and sulci in darker gray. The `FS Regions` overlay loads the Desikan-Killiany Atlas cortical parcellation of the surface as determined by Freesurfer. The information from this parcellation is used to assign names of regions of interest. The `Shadow` options will create a light source in the Matlab figure and shade the brain appropriately so folds are visible.



Metrics

The next panel allows the user to manipulate the data overlays loaded in the previous step and create two new ones. The menu keeps separate configurations for each metric.



Metrics

Minimum Norm Estimates ▾

Time Window (ms)

Start 100

Stop 400

Compute the Mean ▾

Combine via Max ▾

Standardizing

□ Standardize □ Only Mean

Globally ▾

□ Local to FS Regions

Visualizing

☑ Show Hot ▾

● Percentile ○ Absolute

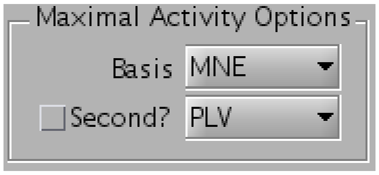
80 90 95

Five Measures of Source Activity

The first three metrics are loaded by the user: the Minimum Norm Estimates of the cortical activity, the phase locking values across the cortex, and it also has room for another metric named custom. Although the default names are preserved, information can be freely loaded into these three topics.

The `Maximal Activity` metric is used to collect the data from the other primary metrics in order to determine the location of the centroids for making the regions of interest. It is based on one of the three original data metrics (the `Basis`). Optionally, another metric can be added in. The data is summed after individual standardizing in the original metric menu so even data with two different scales can be used together.

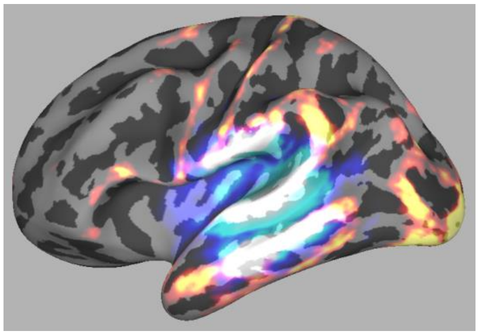
Similarity will be discussed in the Regioning section.



Maximal Activity Options

Basis MNE

□ Second? PLV



Time Window

This interface was designed to summarize data, so by default it will display the mean of the cortical activity measure from 100 to 400. The starts and stops of the time window can be modified by changing the values in the text input fields. The `Compute the {mean, median, max}` option allows the user to change which how the data is summarized for the window.

Multiple fields can be selected by entering multiple starts and stops. For example, if the start times are listed as `100, 500`, and stops `400, 800`, then the program will take the means of the time windows 100 to 400 and 500 to 800 then take the max of these two values. The way the time periods are combined is changed in the `Combined via {mean, median, max}`.

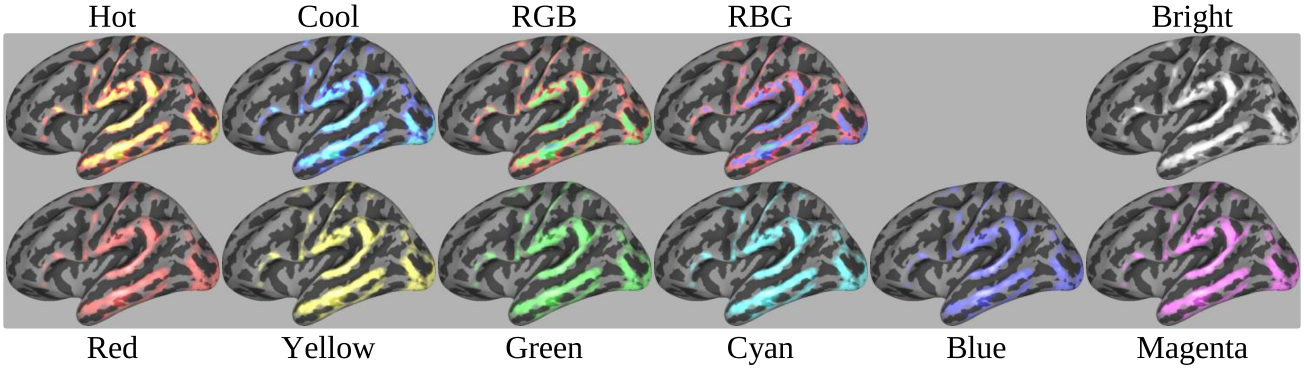
Standardizing

Data sets may be presented on vastly different scales so in combining them it may be important to standardize the measures. By checking the standardize option, the timecourses are subtracted by the mean of all of the timecourses, and then divided by the standard deviation. The adjusted waves can be interpreted with the amplitude “standard deviations from the baseline”. Selecting Only Mean will remove the step in which it divides by the standard deviation.

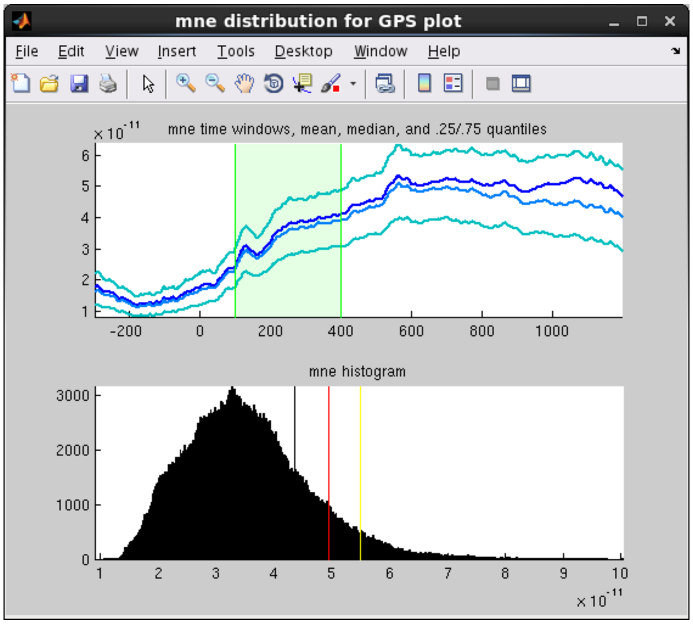
There are many scopes of standardization, accessed through the list starting with `Globally`. `Globally` will use the mean/standard deviation for every time sample in every vertex. `per Vertex` will standardize for each source vertex separately, eliciting the unique shape of each source’s waveform, while `per Time Sample` will standardize in each point in time across the brain, highlighting the waveforms that are consistently higher than others. The `windows` options will standardize each specified time window separately.

Visualizing

The last options for the metric regard visualizing the distribution of activity on the cortical surface. The show checkmark (entangled with the metric’s name in the quick display option) toggles the visibility of the overlay. The metrics are rendered by applying indexed colors to each vertex based on their value. The distribution of color is from black (matching the background color of the brain) to white. In between, the color scale can be based in percentiles or absolute values which can be specified by the user. There is a drop down list of the color schemes, including the six main digital spectrum colors, as well as the standard hot and cool continuums, brightness, and schemes alternating the color on each threshold marker: RGB or RBG. See them below:



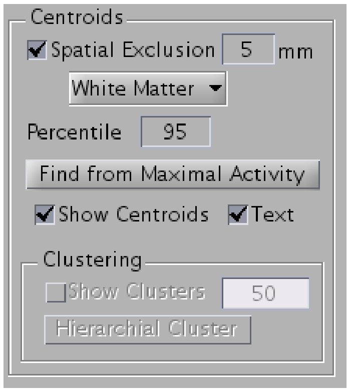
Every time the metrics compute a new mapping, it will produce a chart such as displayed on the left. Although these windows can become overwhelming, they display a summary of the timecourses and distribution of values for the metric. The top chart shows the average timecourse (blue), median (light blue), and .25 and .75 quartiles (seafoam). The histogram below shows how many vertices meet each specific threshold.


mne distribution for GPS plot
File Edit View Insert Tools Desktop Window Help
mne time windows, mean, median, and .25/.75 quantiles
× 10^-11
6
5
4
3
2
1
-200
0
200
400
600
800
1000
mne histogram
3000
2000
1000
0
1
2
3
4
5
6
7
8
9
10
× 10^-11

Centroids

This menu uses the `Maximal Activity` metric to find vertices to seed potential ROIs. Clicking `Find from Maximal Activity`, runs a very quick algorithm to determine vertices across the brain of locally high activity. These vertices will be used as centroids for regions of interest. Use the `Show Centroids` button to draw crosshairs over each point considered a centroid. The `Text shows` automatically generated labels. Centroids are labeled based on their Freesurfer region and the ordered of which was the highest.

There are two primary parameters. `Percentile` controls how many of



Centroids

☑ Spatial Exclusion 5 mm

White Matter

Percentile 95

Find from Maximal Activity

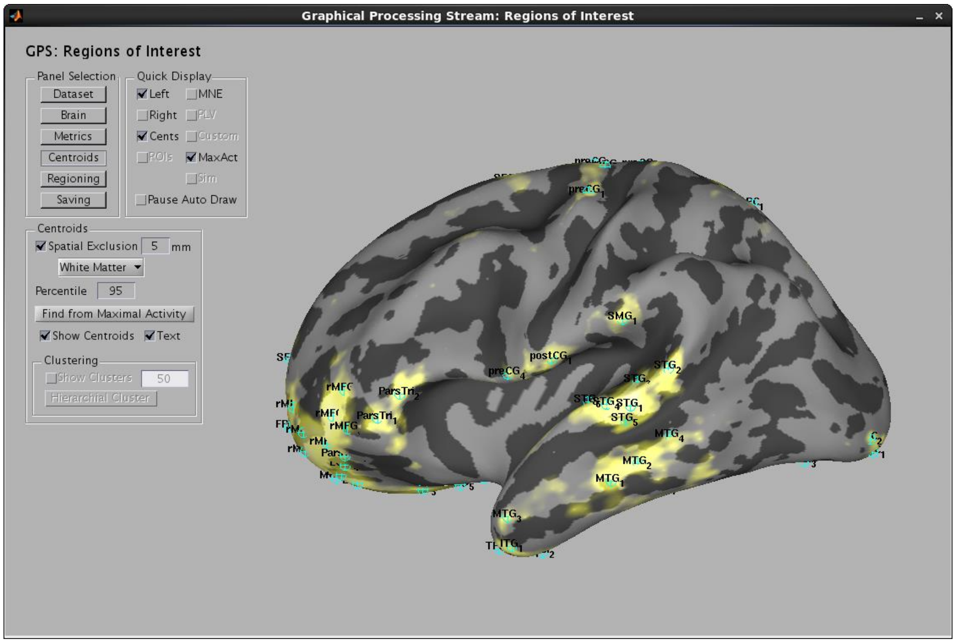
☑ Show Centroids ☑ Text

Clustering

□ Show Clusters 50

Hierarchial Cluster

the vertices above the x percentile of Maximal Activity are eligible to becoming centroids. The algorithm looks through this list from the highest activity to lowest. It selects the centroids from the top of the list one at a time, throwing out candidate vertices that are within the Spatial Exclusion parameter of the selected vertex This step is done so that only locally maximal vertices are selected rather neighboring points.



Graphical Processing Stream: Regions of Interest

GPS: Regions of Interest

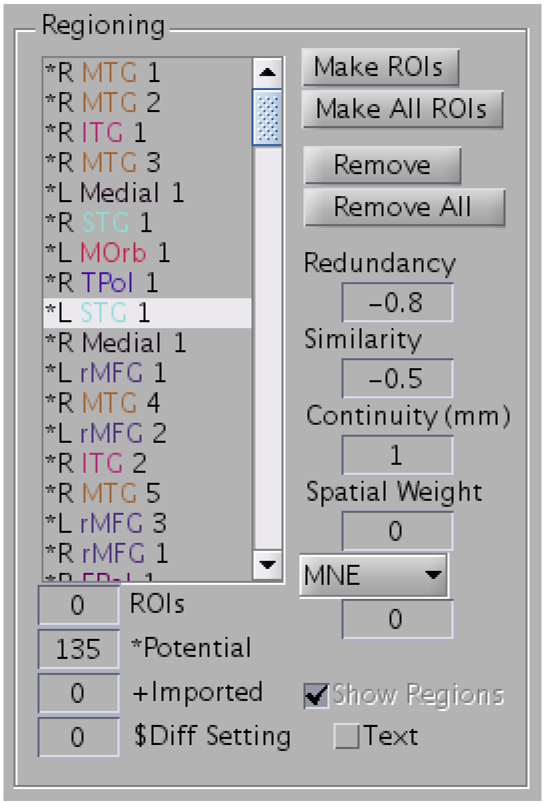
Quick Display: ☑ Left □ MNE □ Right □ PLV ☑ Cents □ Custom □ ROIs ☑ MaxAct □ Sim □ Pause Auto Draw

Centroids: ☑ Spatial Exclusion 5 mm, White Matter, Percentile 95, ☑ Show Centroids ☑ Text

Clustering: □ Show Clusters 50

Creating Regions

Regions of interest can be generated from the list of centroids automatically. There are a variety of parameters used in this step. These parameters place limits on the similarity that are used to define and differentiate ROIs. Points that have measured similarity close enough to centroids are combined to make a region across the cortex. Each region can have no more than 1000 vertices. The `Make ROIs` button will create regions from only selected centroids, while the `Make All ROIs` button will create regions based on all centroids. They can be removed individually or in batch. There is a toggle for showing region patches and labels just like the centroid setting.



*R MTG 1
*R MTG 2
*R ITG 1
*R MTG 3
*L Medial 1
*R STG 1
*L MOrb 1
*R TPol 1
*L STG 1
*R Medial 1
*L rMFG 1
*R MTG 4
*L rMFG 2
*R ITG 2
*R MTG 5
*L rMFG 3
*R rMFG 1

Redundancy -0.8
Similarity -0.5
Continuity (mm) 1
Spatial Weight 0
MNE 0

0 ROIs
135 *Potential
0 +Imported
0 $Diff Setting

☑ Show Regions
□ Text

Parameters

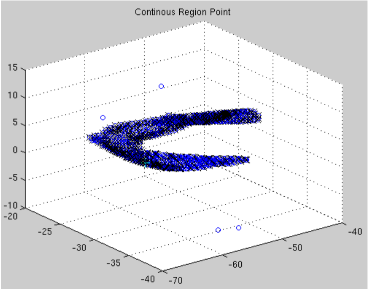
Redundancy: When each ROI is created, centroids that are similar to the selected centroids, and are between this threshold and 0 (zero would be identical to the selected centroid) are thrown out to make sure only unique regions are formed. This is shown as vertices with colors between red and blue on the brain.

Similarity: Vertices on the cortex within this similarity threshold are included within the selected centroid's region of interest. This is shown as vertices with colors between blue and green.

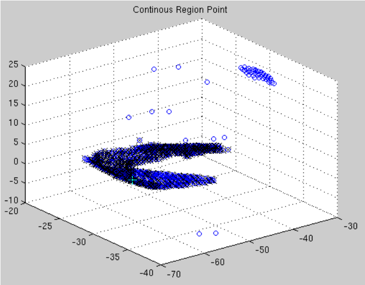
Continuity: The number of millimeters a point must be from other neighbors to be considered in a contiguous region of interest.

Spatial Weight: A value between 0 and 1 that weighs Euclidean spatial proximity between the centroid and vertices. By using this threshold, points closer to the centroid are more likely to be included in the region, and points in other locations of the brain are not thrown out based on redundancy.

Activity Weight (MNE, PLV…): This will weigh the mean activity within the focus time period in the similarity computation. Points with lesser mean activation will be weighted down while points with higher or similarly high activation will be considered more similar.

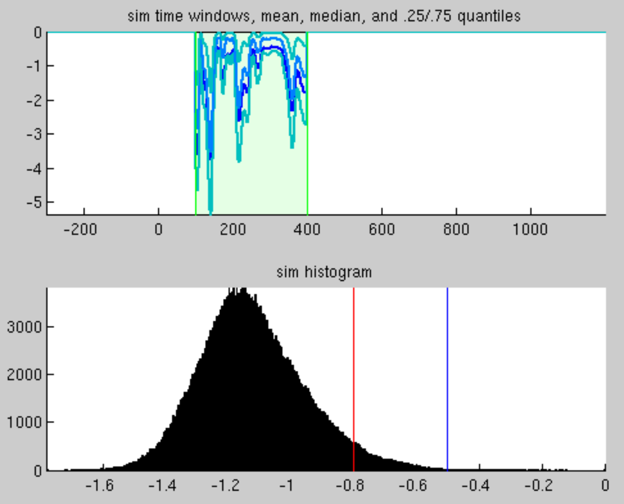


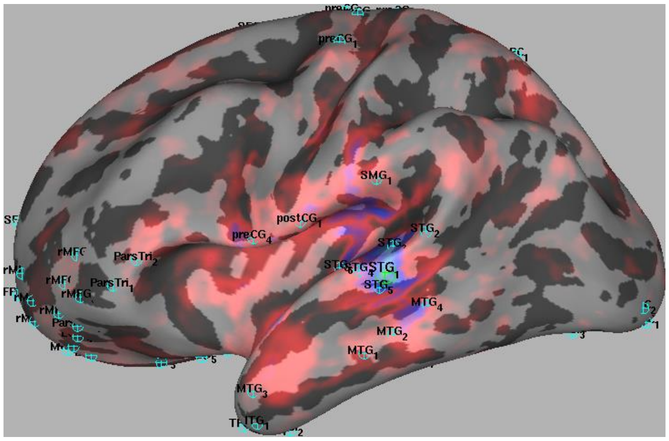
When regions are created, a figure is made showing the vertices that are within the similarity threshold, and highlighting the ones that are considered in a contiguous region starting from the centroid.

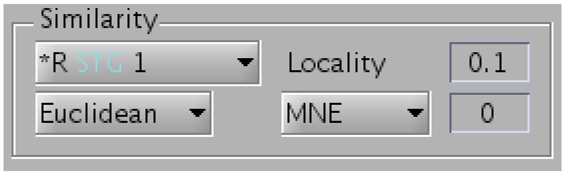


The Similarity Metric

Similarity means two things: It recalls the standardized distance between two points in activity timecourses or it may also include the spatial and activity intensity weight. The first aspect computed is the difference between the MNE cortical activity time courses during the focused periods. Before curves are compared, they are standardized by subtracting the mean and dividing by the standard deviation. This reduces each vertex time profile to a representation based on shape rather than amplitude. These normalized waves are compared to the selected centroid by getting the sum of the difference between their waves, squaring the values, summing the squared differences, adding back these values, then multiplying by negative one to make the scale go from negative infinity to 0. Points with 0 distance must have identical waveforms, otherwise the lower (more negative) the similarity is, the more different the waveforms are. Units of this metric are roughly considered normalized standard deviations.







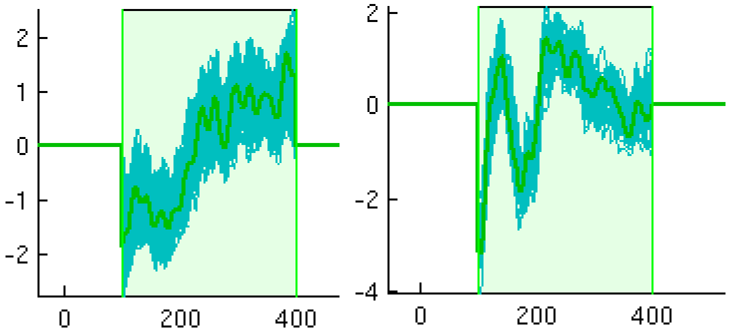
Similarity

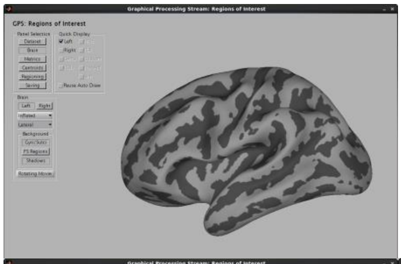
*R STG 1 ▾ Locality 0.1

Euclidean ▾ MNE ▾ 0

This can be visualized in the metrics menu after having selected centroids. If the centroid list is empty it may try to throw errors until the list is populated again.

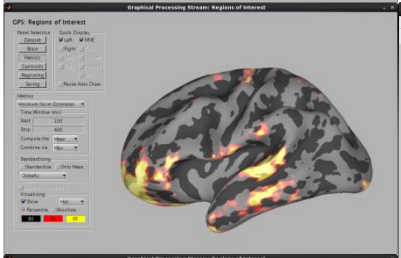
If the spatial or activity intensity weights are above 0, they will be factored in appropriately. Waves that fall in the Similarity threshold are combined to form a cohort to be tested for continuity and formed into regions. These two timecourse charts show the centroid timecourse (green) and the timecourses of vertices with waveforms within 0.5 similarity to the centroid.

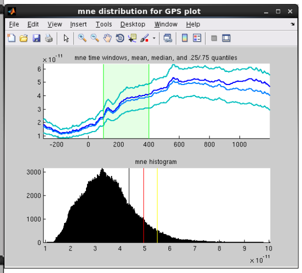




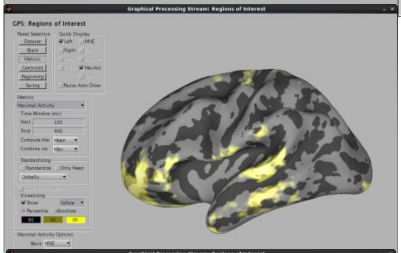
Procedure

1. Select the study, subject brain, and condition to make regions for.
2. Load the metrics that will be used, at least including MNE cortical activity.

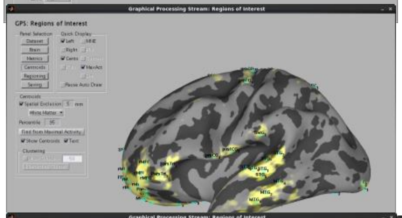



mne distribution for GPS plot
mne time windows, mean, median, and .25/.75 quantiles
mne histogram

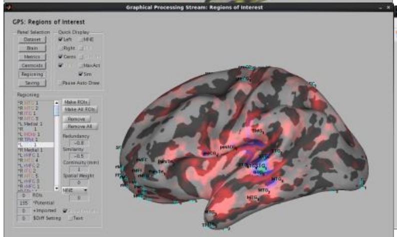
3. Visualize the MNE cortical activity.

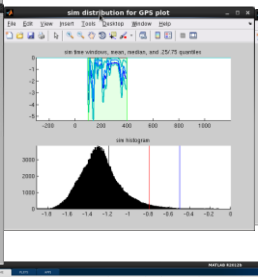


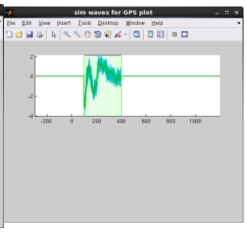
4. Generate the Maximal Activity metric from one or more datasets.



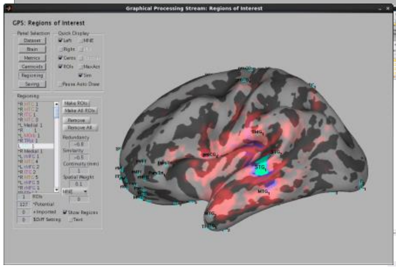
5. Generate a list of centroids as candidates to seed regions of interest.

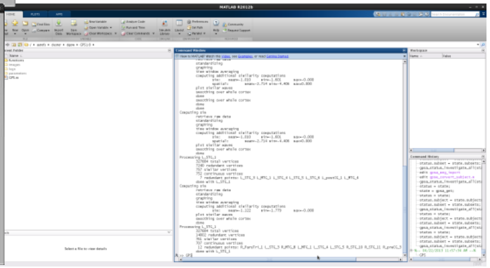



sim distribution for GPS plot
sim time windows, mean, median, and .25/.75 quantiles
sim histogram

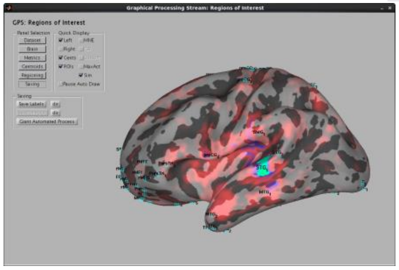


6. Select necessary regions and examine similarity.





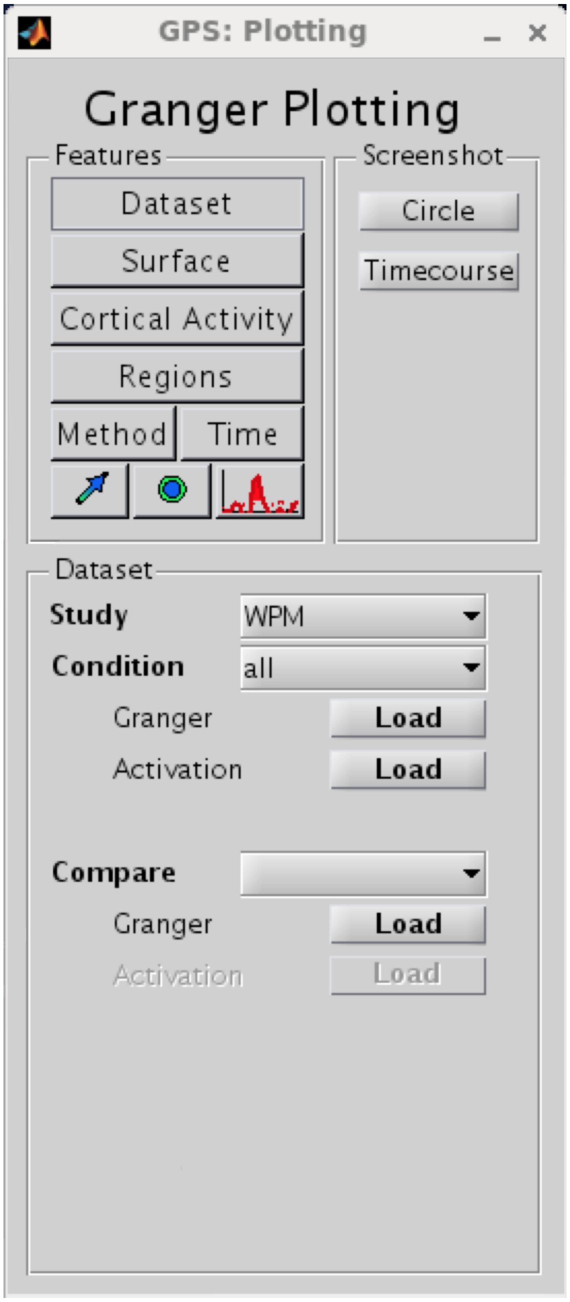
7. Create (All) ROIs. This will automatically run.



8. Save labels in the saving menu. This step will also save a screenshot of the current view and save a .mat file containing data useful for downstream analysis.

Chapter 7: Plot Drawing Interface

The plot drawing interface is a tool that loads the data produced by GPS Analysis and displays graphs of Granger causality. Below, it is outlined each of the menus and the effects of each option. This interface can be operated without MNE or Freesurfer as long as the subject's MRI files have already been processed and the final Granger results have been computed.



Study WPM

Condition all

Figure 7.1 Granger Plot Drawing Open

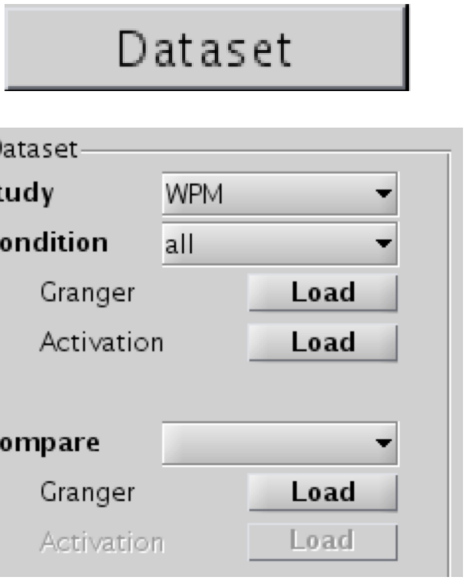
There are 3 main boxes on the screen. The buttons in “Features” select different menus to appear down below. The box labeled “Dataset” in Figure 7.1 will display options for each feature. The “Screenshot” box just contains fast shortcuts to take pictures of the circle & surface plots or the timecourse plot.

Besides this menu figure, GPS: Plot Drawing has three more figures. The Circle or Surface figure displays rendered graphical or neural displays of the data. The Timecourse figure shows time courses indicated in the last feature button. At start, they are turned off by default but you can change them in the menus.

The data figure will hold all of the data you select to load in the dataset menu. It will also contain analysis made by the GUI. The reason these variables are stored in a separate figure window is because, otherwise, the primary figure would be overburdened with memory-wanting variables and it would act very slow. Do not close this window or you will lose your session’s data. It is safe to minimize it.

Figure 7.2 Data figure

Loading a Dataset



Study: WPM

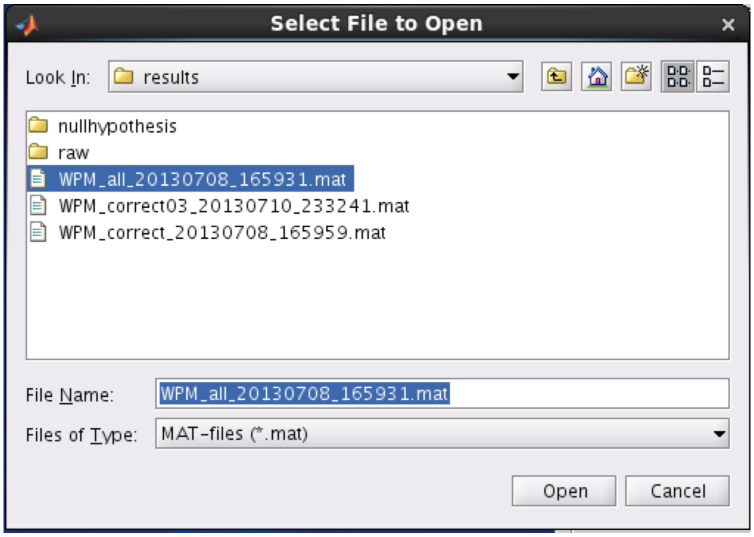
Condition: all

Compare:

Figure 7.3 Dataset button and menu

The Dataset menu provides functions for the user to load granger analysis for the conditions of a study. The study list is populated by looking at the GPS parameters directory just like in GPS Analysis. The condition list shows conditions for that study. Since conditions specify which brain they have data analysis on, it can automatically figure out which freesurfer files to load.

Clicking on the Load button next to Granger will open a dialog to select the file in which the Granger data is held. If everything is built in GPS and the Analysis functions ran okay, then the dialog should point to the correct file to open.



Look In: results

nullhypothesis
raw
WPM_all_20130708_165931.mat
WPM_correct03_20130710_233241.mat
WPM_correct_20130708_165959.mat

File Name: WPM_all_20130708_165931.mat

Files of Type: MAT-files (*.mat)

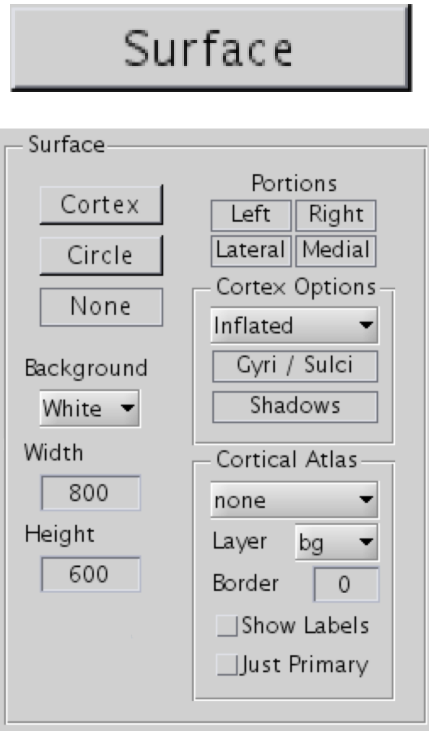
Figure 7.4 Dataset file selection dialog

This folder is the condition.granger.dir/results folder. The original granger analysis is in the raw directory and can also be opened by GPS: Plot Drawer. The null hypothesis data is in the corresponding folder but takes too much time to load so that extra preparation step was built into the GPS: Analysis routine.

The activation loading function will find the MNE cortical activation maps generated in the MNE stage of the analysis. Right now, there is not support for comparing activation maps so the comparison condition does not have that option.

The compare section has a dropdown list of all of the conditions compatible with the selected condition for comparison. For instance, both conditions must be analyzed with the same cortical surface.

Rendered "Surface" Plots



Background
White

Width
800

Height
600

Inflated

none

Layer bg

Border 0

Figure 7.5 Surface button and menu

In order to see the neural activity on the brain or see nodes with granger causality flowing between them, choose a surface in the surface menu. The cortical surface can display activation as well as be drawn on by the visualization functions to illustrate causality. The circle display just shows each region as a label around a circle and can display arrows or node sizes.

Options

- Background: Allows you to choose the color for the background of the render.
- Width: Attempt to make the plot a fixed width long.
- Height:Attempt to make the plot a fixed width tall.
- Portions:
  - Left/Right: Include the left and/or the right hemisphere.
  - Lateral/Medial: Display the surfaces from either perspective
- Cortex Options
  - Surface: Default "Inflated" this specifies which FS built cortical surface to view
  - Gyri/Sulci: This option clarifies whether or not to partition the brain into gyri and sulci by brightness.
  - Shadows: Determines whether the rendering engine should spend time making shadows. Turn this off if you want a more cartoony approach.
- Cortical Atlas
  - Freesurfer automatically generates a few atlases of the subject's brain such as coarse descriptions of primary anatomical areas. If you select an option other than

none from the dropdown, it will draw an overlay of these regions on the cortical images.

- Layer: Whether or not you want the atlas's features to be shown on the foreground (blended with cortical activation), background (blended with the gyri/sulci overlay) or on top of it all.
- Border: If you want thicker borders to the regions, write a number between 1 and 10 in this box. For instance, your GPS Analysis processed ROIs will be available as an atlas and you can visualize it in this rendering scheme.
- Show Labels: When this box is checked it will show the names of the labels.
- Just Primary: Turn this option on if you are selecting just one or a few of the ROIs from the "Regions" menu and want to map only these primary ROIs on to the cortical map.

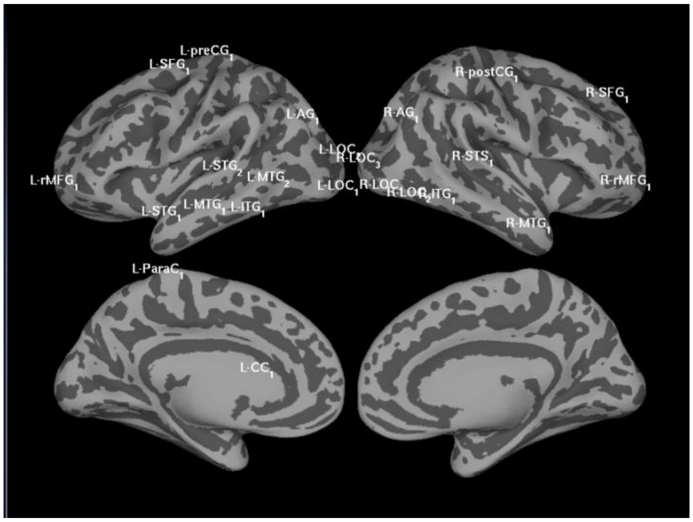


Figure 7.6 A typical cortical surface display

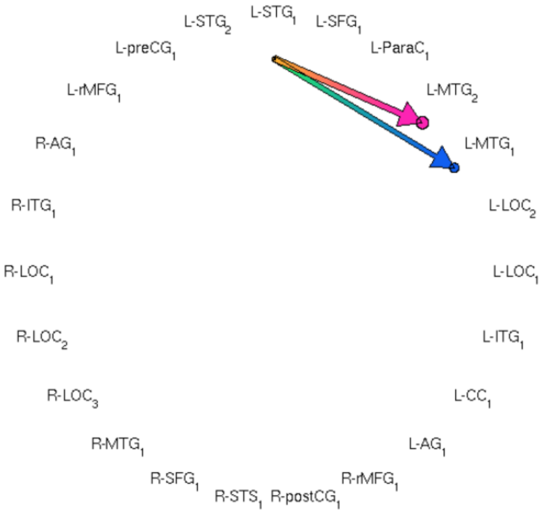
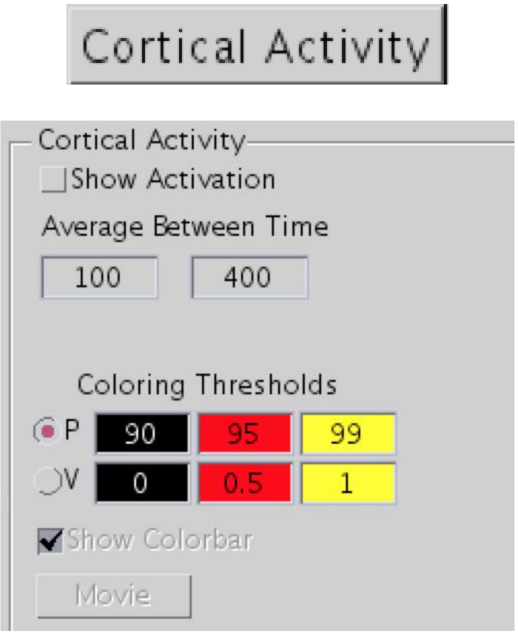


Figure 7.7 Circle representation, showing granger causality directions as arrows

Cortical Activity



Cortical Activity

Cortical Activity

□ Show Activation

Average Between Time

100 400

Coloring Thresholds

● P 90 95 99

○ V 0 0.5 1

☑ Show Colorbar

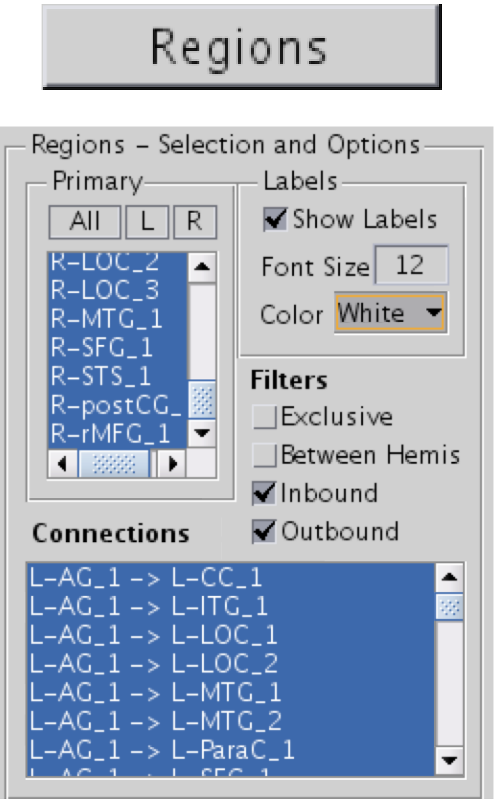
Movie

Figure 7.8 Cortical Activity button and menu

This menu works only if you have loaded a cortical activity basis for the primary condition. If you check the box “Show Activation,” the program will render cortical activation using a standard heat map on the cortical surface. It will average it in the millisecond time window you specify. Activity can be colored by percentage (P) thresholds or absolute value (V) thresholds.

At this monment the Show Colorbar box is disabled.

Regions, selection and labels



R-LOC_2
R-LOC_3
R-MTG_1
R-SFG_1
R-STS_1
R-postCG_
R-rMFG_1

☑ Show Labels
Font Size 12
Color White

□ Exclusive
□ Between Hemis
☑ Inbound
☑ Outbound

L-AG_1 -> L-CC_1
L-AG_1 -> L-ITG_1
L-AG_1 -> L-LOC_1
L-AG_1 -> L-LOC_2
L-AG_1 -> L-MTG_1
L-AG_1 -> L-MTG_2
L-AG_1 -> L-ParaC_1

Figure 7.9 Regions button and menu

Loading all of the granger connections at once can be daunting and incomprehensible. Thereby, GPS allows you to select just a subset of your data to look at. The primary box shows all of the ROIs of the condition you are analyzing. By selecting ROIs here, only granger connections involving these ROIs will be displayed. The All, L, and R buttons select (or deselect) the whole list, the left side, or the right side respectively.

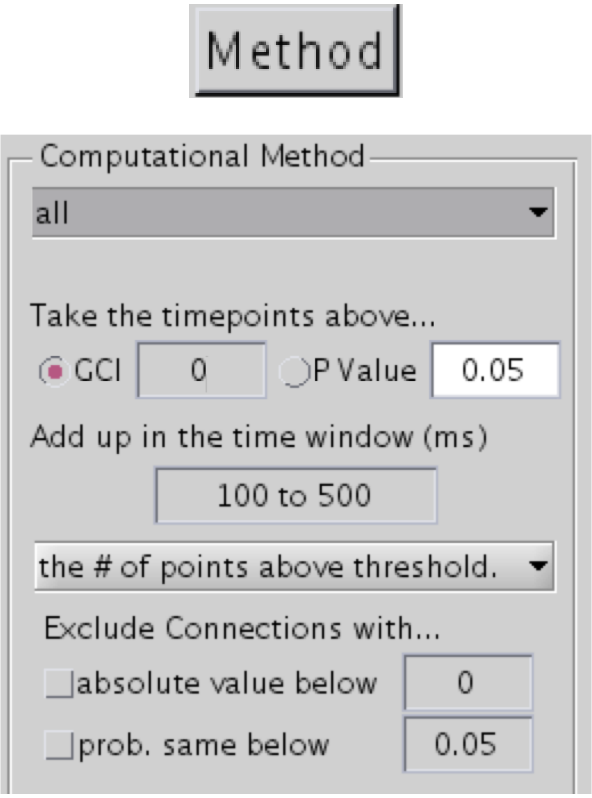
The connections list contains a listing of all possible pairs involving the selected ROIs from the primary listing. If you select the exclusive filter, it will only show possible pairs involving combinations among selected ROIs. You can choose to ignore outbound or inbound connections from your selected ROIs by unchecking that box. Checking the box Between hemis will only display connections that stay in one hemisphere (eg. Left to left).

The labels box is a secondary way to label your regions, which options for font size and font color.

Granger Process

The next two buttons open menus that help you manipulate the Granger connectivity data.

Methodology



Computational Method

all ▾

Take the timepoints above...

● GCI 0 ○ P Value 0.05

Add up in the time window (ms)

100 to 500

the # of points above threshold. ▾

Exclude Connections with...

□ absolute value below 0

□ prob. same below 0.05

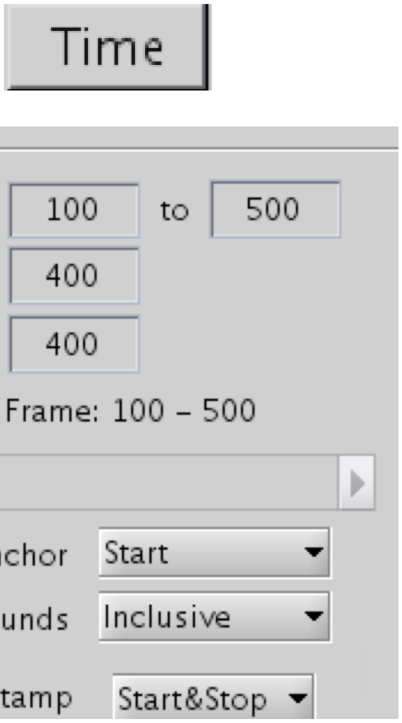
Figure 7.10 Method button and options

This option list helps you to properly format your data for visual analysis.

Options:

- *Dropdown*: The dropdown list lets you specify whether you are seeing your primary condition, or your comparison condition.
- *GCI*: Specify that time points are significant if the Granger Causality Index is above a certain value. 0 is the baseline GCI, but numbers around 0.25 generally work in practice. However, once you have run significance testing use P values.
- *P Value*: Timepoints can be evaluated on how unusual they are from the null hypothesis tests.
- *Time Window*: This window cannot be edited, but it displays the information from the time page.
- *Dropdown 2*: This allows you to select whether you are counting the number of significant timepoints, or whether you want to add suprathreshold values together.
- `Exclude connections with…` This helps you to exclude weak connections from visualization. The `prob. same below` option only works when there are p values for a primary and comparison condition.

Time



Timing

Window 100 to 500

Duration 400

Interval 400

Viewing Frame: 100 – 500

Frame Anchor Start

Frame Bounds Inclusive

□ Timestamp Start&Stop

Figure 7.11 Time button and options

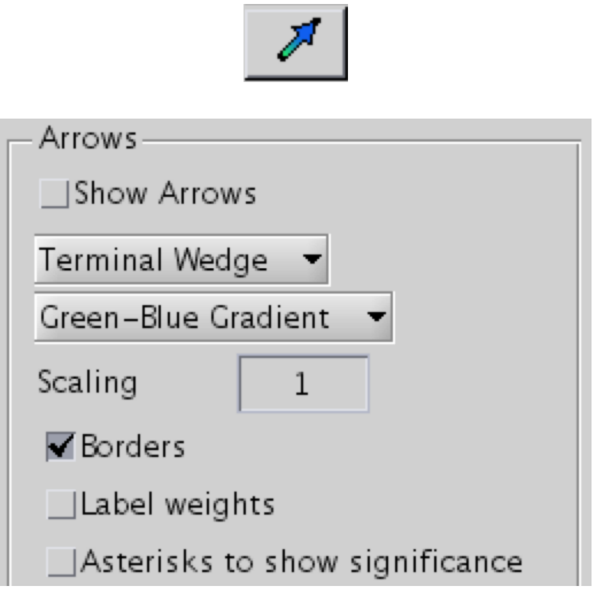
This feature allows you to specify which time window you are examining. In practice, you will not modify this often. If you specify lower durations and intervals you can see more slices of the granger interaction and you can use the slide to jump between time periods.

The timestamp option at the bottom is useful for understanding which time points are actually going into your visualizations.

Granger Visualizations

There are three visualizations available to examine the data:

Arrows



Arrows

□ Show Arrows

Terminal Wedge ▾

Green–Blue Gradient ▾

Scaling 1

☑ Borders

□ Label weights

□ Asterisks to show significance

Figure 7.12 Arrows button and options

This feature set allows you to visualize Granger interactions as arrows. Arrows are useful in showing the directionality of signals between ROIs

Options

- *Show Arrows:* Toggles the display on the cortical or circle surface
- *Terminal Wedge….:* Allows you to choose among different arrow styles.
- *Green-Blue Gradient:* Allows you to choose among different arrow colors. The green/blue option is generally the most used option. Green represents signals leaving the region, while blue represents signal arriving at the region.
- *Scaling:* This option allows you to modify the size of the arrow in order to enhance visualization; however it is advised that users keep the same scale across analysis.
- *Borders:* Selecting this box will add borders to the arrows.
- *Label Weights:*Check if you want values indicating magnitude displayed in each arrow.
- *Asterisks to show significance*:If you are doing a comparative test, you can click this and it will put asterisks in arrows based on if that relation is statistically important.

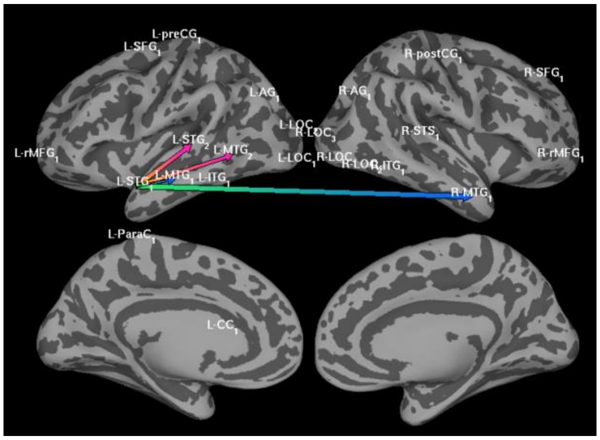
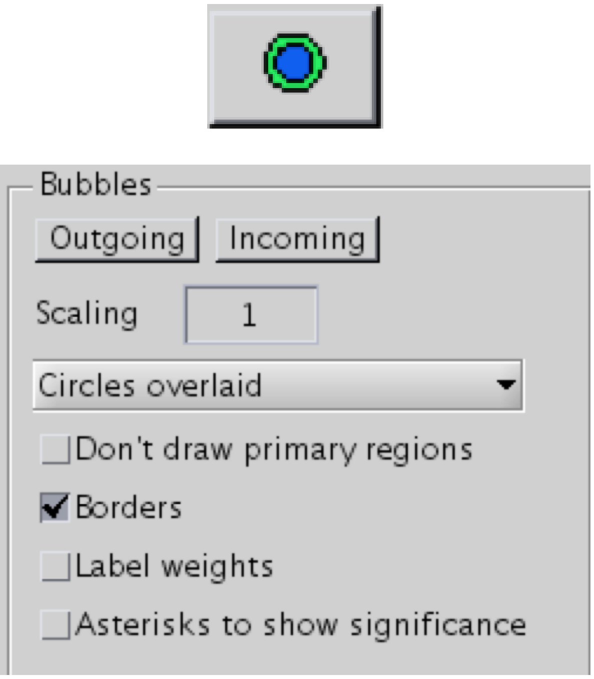


Figure 7.13 Cortical surface with arrows

Figure 7.13 shows what the arrows look like on a cortical surface. In this case, it is showing a comparative analysis between the "all" and "correct" conditions. Green-Blue arrows show higher "all" activity, Yellow-Magenta arrows show higher "correct" activity.

Nodes, "Bubbles"



Bubbles

Outgoing Incoming

Scaling 1

Circles overlaid

☐ Don't draw primary regions

☑ Borders

☐ Label weights

☐ Asterisks to show significance

Figure 7.14 Nodes button and options

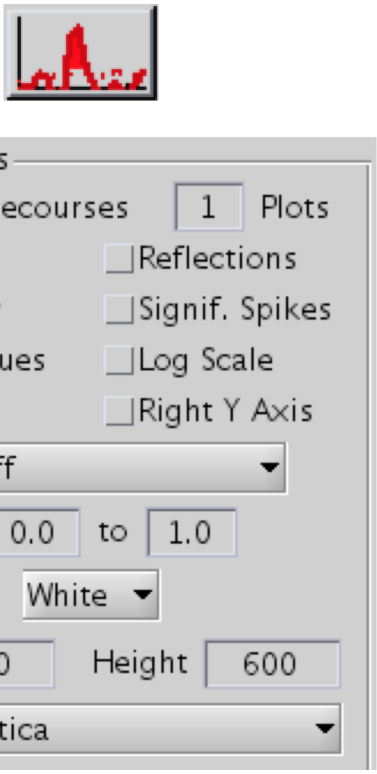
Instead of arrows, values can be displayed as circles where the regions are located. They will be colored the same way as the arrows but other options can change their behavior.

Options

- *Outgoing:* Toggle button for whether or not to show the sum of granger connection indices (or the count of, depending on your method) starting at each node.

- *Incoming:* Selecting this box will show the sum of granger connection indices ending at each node.
- *Scaling:* This section allows you to input a desirable scale for the circles in order to enhance visualization; however it is advised that users keep the same scale across analysis.
- *Circles overlaid…* This menu presents with options of different ways that outgoing and incoming summations can be visualized.
- *Don't draw primary regions:* Checking this box will only display circle on the ROIs that are influenced by the selected ROIS, thus there will be no circles on top of selected ROIs
- *Borders:* Checking this box will draw borders around the circles
- *Label weights:* Add text indicating the values. Shown around label. It can be very effective for giving summary statistics.
- *Asterisks…:* Indicates comparative significance in circles/labels.

Time Courses



Timecourses

□ Show Timecourses 1 Plots

☑ Fill □ Reflections

□ Tips Only □ Signif. Spikes

□ Plot P Values □ Log Scale

□ Flip Y Dir □ Right Y Axis

Legend Off

Y Bounds 0.0 to 1.0

Background White

Width 800 Height 600

Font Helvetica

Figure 7.15 Timecourses button and menu

. There are a large number of options for this feature set. It will display the time courses for all of the connections selected in the Regions menu. The solid line will show the GCI (or p-value, as specified in the Method menu) and the dashed line will show the criteria (eg. a p-value of no more than 0.05).

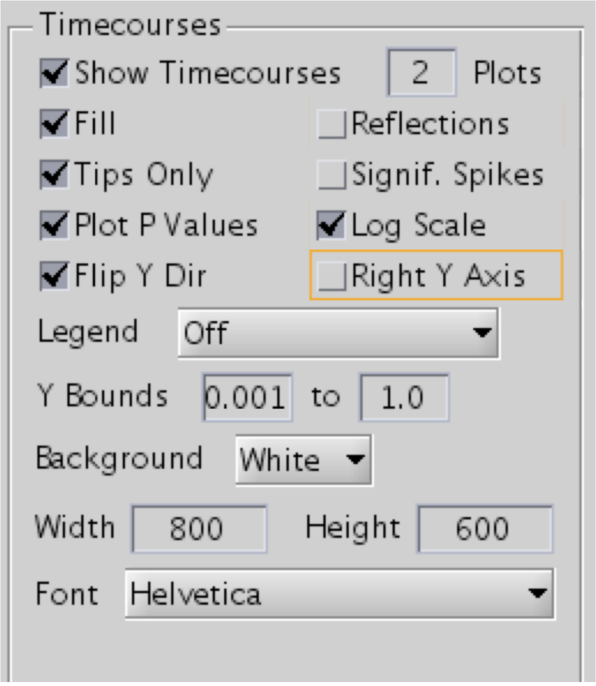
Options:

- *Show Timecourses*:Checking this box will open a timecourse figure.

- *[ ] Plots*: Allows you to input the number of plots to be generated, which can be useful when viewing a lot of connections.
- *Fill*: Fill the space the experimental values are above the criteria.
- *Reflections*: Plot the reverse directions as well, on a flipped chart if you have also selected tips only.
- *Tips Only:* Selecting this option will only draw values within the criteria line, which can make the chart much more tractable.
- *Signif. Spikes*: Draw vertical lines where timepoints are significant
- *Plot P Values:* Change the legend to p values as well as the nature of some of the functions.
- *Log scale*: Change the y axis to a logarithmic scale.
- *Flip Y Dir:* Flip the direction of the Y axis
- *Right Y Axis:* Show the Y axis on the other side of the screen

- *Legend:* This menu allows user to choose where legend should be positioned within the picture.
- *Y Bounds:* The minimum and maximum for the plot
- *Background:* This menu allows user to choose the background color for the graph.
- *Width:* The approximate width of the plot
- *Height:* The approximate height of the plot
- *Font:* What font to render the names in. Some journals require specific fonts. Be careful, this list is generated from your computer but not all fonts listed may render corrected in Matlab.

The following, are graphs for the sample data's all and correct condition which the timecourse settings to make those plots.



Timecourses

☑ Show Timecourses 2 Plots

☑ Fill □ Reflections

☑ Tips Only □ Signif. Spikes

☑ Plot P Values ☑ Log Scale

☑ Flip Y Dir □ Right Y Axis

Legend Off

Y Bounds 0.001 to 1.0

Background White

Width 800 Height 600

Font Helvetica

Figure 7.16 Timecourse options for Figure 7.17

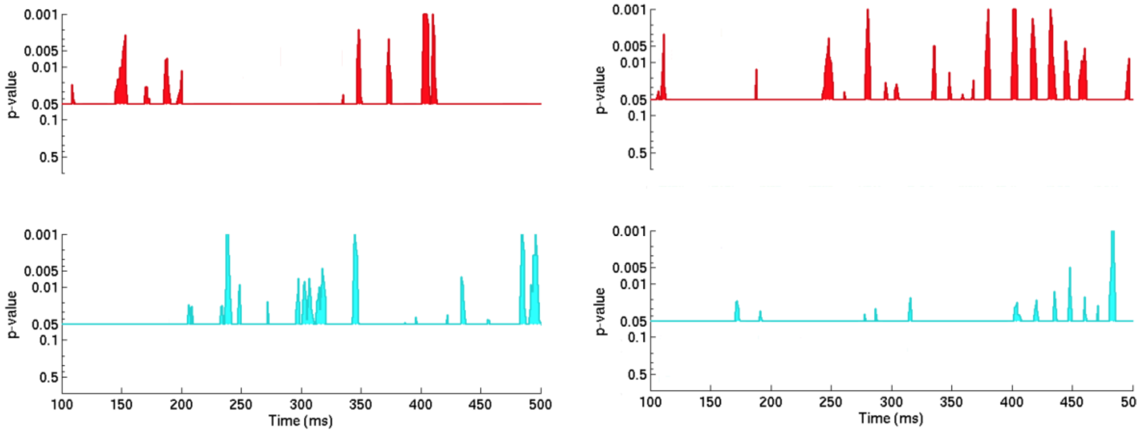


Figure 7.17 Timecourse plots for L-STG to L-MTG1 (Red) and L_MTG2 (Cyan) for WPM "all" (Left) and "correct" (Right) conditions.

Appendix 1: Remote Connecting

This section applies to Martinos Center users only.

In order to access the graphical processing stream from a personal computer or a machine not directly connected to the Martinos network, one needs to build a network bridge to the center. There are a few different ways to remotely connect; this section will highlight the most used ones. This presumes that you have access to a Martinos network computer Linux computer. This manual should provide you all of the necessary information but in case you run into any problems or want more options you may consult the Martinos documentation for remote connections.

http://www.nmr.mgh.harvard.edu/martinos/userInfo/computer/remoteAccess.php

Secure Shell (SSH)

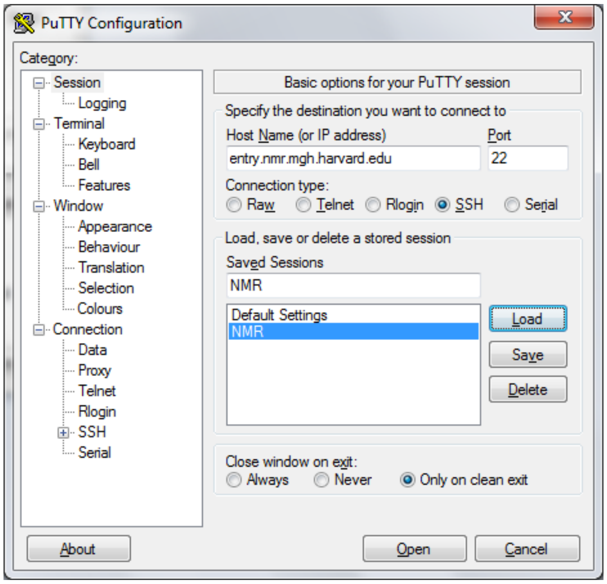
The simplest way to connect to a Martinos network computer is using the Secure Shell protocol, shortened as SSH. This will open a session identical to operating a terminal (shell) client on the Linux machine itself.

Windows

Users of the Windows operating system will need to use PuTTY or a similar SSH client to connect to a computer on the Martinos network. This may be downloaded here:

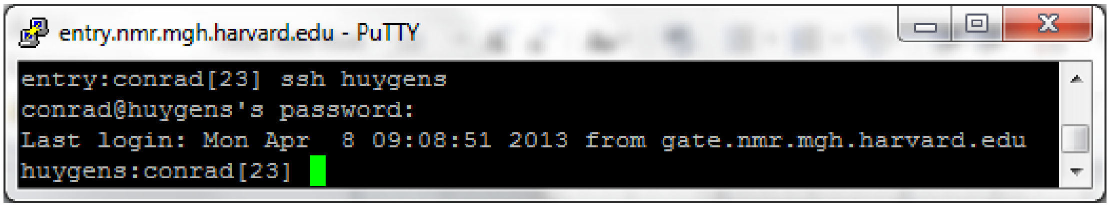
http://www.chiark.greenend.org.uk/~sgtatham/putty/download.html

The first step in connecting is to establish a session with the Martinos network gateway, that is the servers `door`, `entry`, or `gate`. Do not do analysis on these computers, but use this to get into the network. Open up PuTTY. Specify the hostname as `<server>.nmr.mgh.harvard.edu` and the port as number 22.



Host Name (or IP address): entry.nmr.mgh.harvard.edu
Port: 22
Connection type: ○ Raw ○ Telnet ○ Rlogin ● SSH ○ Serial
Saved Sessions: NMR
Default Settings
NMR
Close window on exit: ○ Always ○ Never ● Only on clean exit

Enter your username and password. Once you are connected, directly connect to the computer by using the `ssh` command within terminal. The command is `ssh <servername>`. You will be prompted to enter your password again.

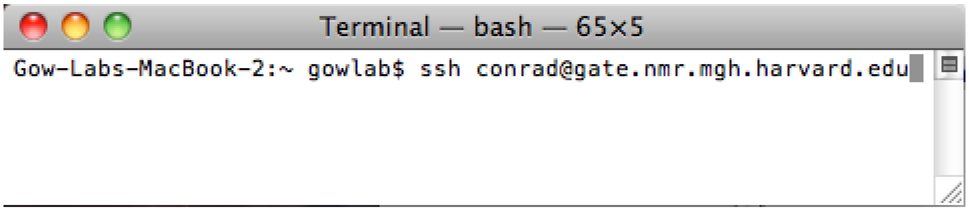


```
entry:conrad[23] ssh huygens
conrad@huygens's password:
Last login: Mon Apr  8 09:08:51 2013 from gate.nmr.mgh.harvard.edu
huygens:conrad[23]
```

Macintosh and Linux

It is much easier to connect on a Macintosh or Linux computer. Since they are built on a Unix kernel and have similar design elements, you can connect to the Martinos network with the native Terminal program. To connect to an internal server connect to a gateway first. The command to connect is

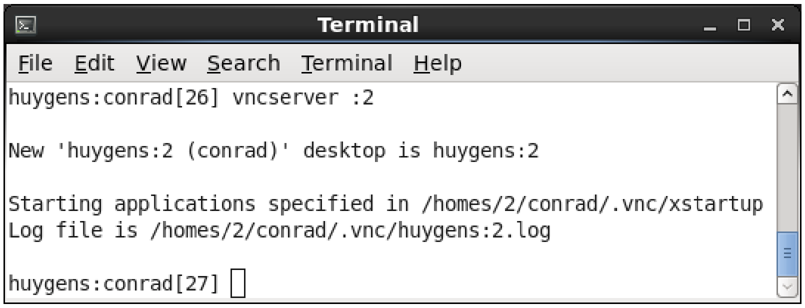
```
ssh <username>@<server>.nmr.mgh.harvard.edu
```



```
Gow-Labs-MacBook-2:~ gowlab$ ssh conrad@gate.nmr.mgh.harvard.edu
```

Virtual Network Computing (VNC)

This approach will enable you to open a desktop session on the remote computer that will appear as a window. In order to start a VNC session you may need to set it up your VNC parameters on your user account in the Martinos network. To start a session, open a terminal to the computer that you want to host the session or SSH into that computer. Start the VNC server by typing the command `vncserver :<num>`, where the number is a value between 1 and 99 that no other user will use. This server will create a session in the remote connecting port of that number.

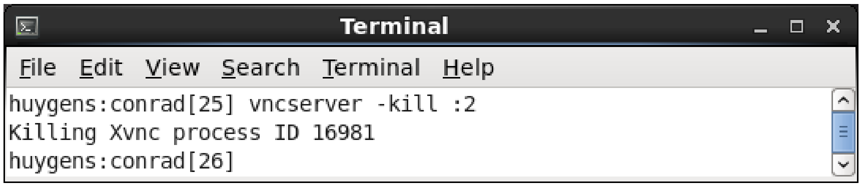


```
huygens:conrad[26] vncserver :2

New 'huygens:2 (conrad)' desktop is huygens:2

Starting applications specified in /homes/2/conrad/.vnc/xstartup
Log file is /homes/2/conrad/.vnc/huygens:2.log

huygens:conrad[27]
```

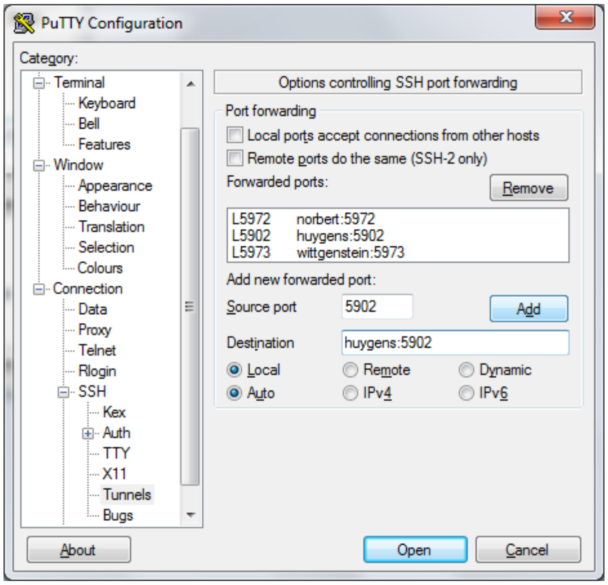


```
huygens:conrad[25] vncserver -kill :2
Killing Xvnc process ID 16981
huygens:conrad[26]
```

In order to terminate an existing vncserver connection, terminate the process using the same command as before but adding the kill option: `vncserver -kill :<num>`

Windows

Back at the computer that is opening the remote connection, you will need to open an SSH session that bridges the VNC connection and then open a VNC viewer. Load the previous session information in which you connect to a Martinos gateway. In the configuration, go to the options for `Connection/SSH/Tunnels` and add a new forwarded port whose source port is `59XX`, in which the number you choose above fills the tens digit. The destination is the desktop you started the vncserver session at then the appropriate `59XX` number again. Add this to the list of forwarded ports, save the session and go.



Options controlling SSH port forwarding

Port forwarding

□ Local ports accept connections from other hosts
□ Remote ports do the same (SSH-2 only)

Forwarded ports:

```
L5972    norbert:5972
L5902    huygens:5902
L5973    wittgenstein:5973
```

Add new forwarded port:

Source port: 5902

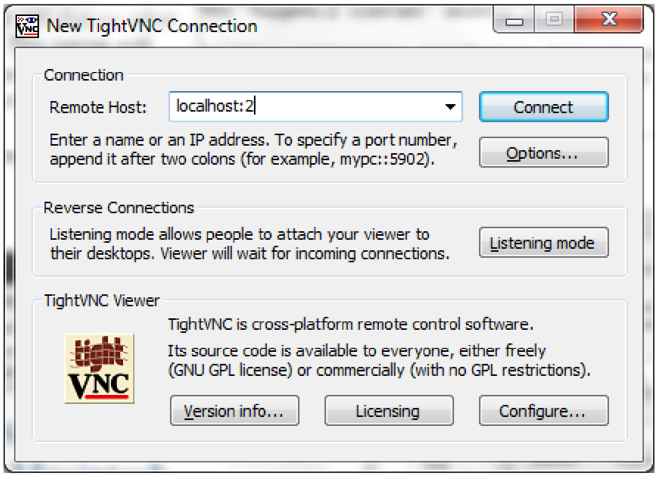
Destination: huygens:5902

● Local ○ Remote ○ Dynamic

● Auto ○ IPv4 ○ IPv6

Now, your computer will need a program that can open VNC sessions. One such program is called Tight VNC. Connect to the remote host `<desktop>:<num>` and enter your VNC password. Note that when you first use VNC you will set up your VNC password and this does not need to change –unlock your Martinos account password. Click OK and the program will open a remote desktop session.

http://www.tightvnc.com/



Connection

Remote Host: localhost:2

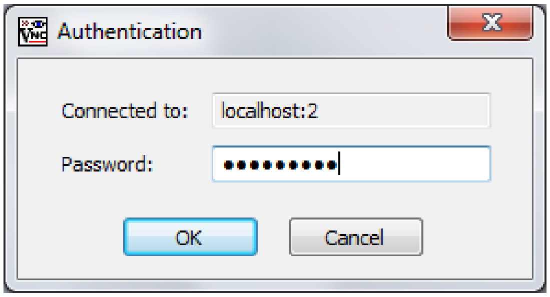
Enter a name or an IP address. To specify a port number, append it after two colons (for example, mypc::5902).

Reverse Connections

Listening mode allows people to attach your viewer to their desktops. Viewer will wait for incoming connections.

TightVNC is cross-platform remote control software.

Its source code is available to everyone, either freely (GNU GPL license) or commercially (with no GPL restrictions).

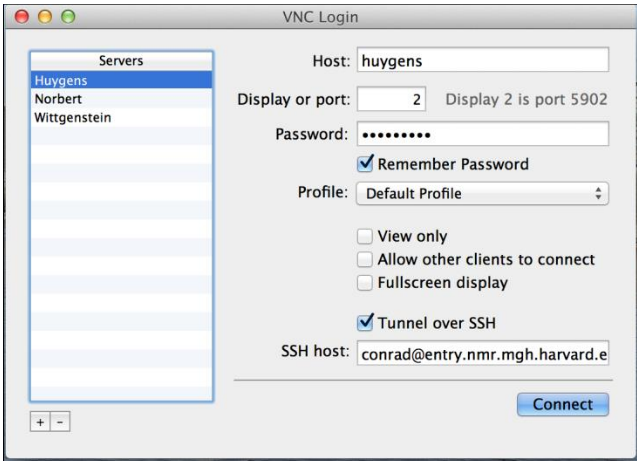


Connected to: localhost:2

Password: •••••••••

Macintosh

Chicken of the VNC offers a much easier client to connect to VNC sessions. The SSH connection is provided by the program. Just enter the destination computer, connection port number, VNC password, and toggle the SSH options and enter the SSH host as `<username>@<server>.nmr.mgh.harvard.edu` . When the session starts it will prompt for your Martinos center password.



Host: huygens

Display or port: 2 Display 2 is port 5902

Password: •••••••••

☑ Remember Password

Profile: Default Profile

□ View only
□ Allow other clients to connect
□ Fullscreen display

☑ Tunnel over SSH

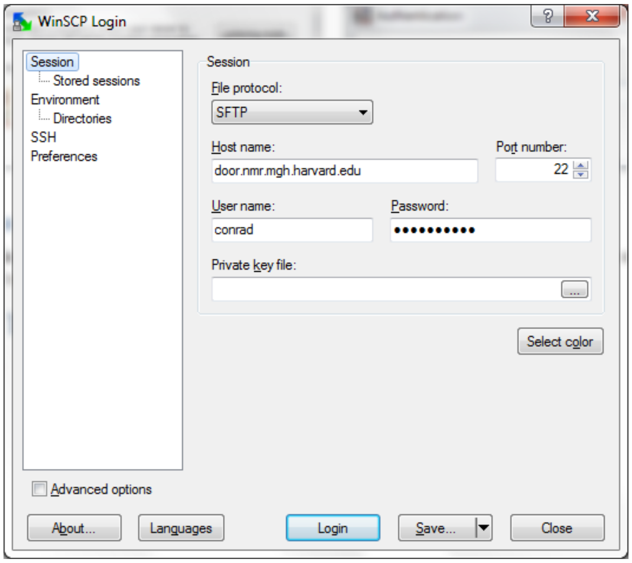
SSH host: conrad@entry.nmr.mgh.harvard.e

http://sourceforge.net/projects/chicken/

File Transfer Protocol (FTP) – Windows

In order to transfer files between the Martinos network and you computers you will want to use a file transferring client. On Windows computers, WinSCP offers a great client for crossing servers. You will want to connect to one of the gateway servers.

http://sourceforge.net/projects/winscp/



WinSCP Login

Session

File protocol: SFTP

Host name: door.nmr.mgh.harvard.edu

Port number: 22

User name: conrad

Password: ••••••••••

Private key file:

□ Advanced options

Appendix 2: Parameters

The study, subject, and condition parameters are collected into standardized structures in the processing suite. They are edited using the Structure Editing Interface as described in Chapter 6. They are saved in a Matlab structure hierarchy. Below is a description of each parameter and the default.

Common Parameters

`name` – The name of the study/subject/condition.
`study` – The name of the study, used to access the folder holding the parameters.
`type` – The type of parameter this is. "`study`", "`subject`", or "`condition`"
`last_edited` – A timestamp to the last time the parameter file was saved.
`version` – The version of GPS that the parameter file is updated to.

Study

`average_name` – The name of the average subject, usually `<study name>`_ave.
`basedir` – The directory holding the signal and analysis information for the study. Note: modifying this will not change the other directory variables.
`blocks` – The list of all blocks, this makes the default for the subject's list of blocks.
`subjects` – The list of all subjects. Remove bad subjects from this list when doing group analysis.
`conditions` – The list of all conditions for the study.
`mri` – This is a substructure with more variables pertaining to the cortical analysis
`rawdir` – The directory to contain the raw MRI recordings, usually `<basedir>/MRIraw`.
`dir` – The directory with the Freesurfer reconstructions, usually `<basedir>/MRI`.
`meg` – his is a substructure with more variables pertaining to the MEG recordings
`dir` – The directory containing the MEG recordings and MNE results, `<basedir>/MEG`.
`raid_pi` – The name of the folder in the MEG RAID system associated with the PI.
`sample_rate` – The standard sample rate for the study, expected 1200 Hz
`mne` – timing and specific constraints for constructing the sensor to cortex mapping
`dir` – The directory containing study MNE files. `<basedir>/MNE`.
`flag_depth` – Whether or not to apply depth weighting in the MNE analysis, default 1.
`flag_emptyroom` – Whether or not the compute the covariance using emptyroom recordings or the pre-trial period. Default 1. Expected emptyroom files: `<subject.meg.dir>/MEG/raw_data/<subject.name>_emptyroom_raw.fif`
There are 10 more parameters in pairs that mark time boundaries relative to the onset of the trial events in milliseconds.
`start/stop` – The trial envelope, default: -300 to 1200
`focusstart/focusstop` – The most important part of the trial for analysis, default: 100 to 400
`basestart/basestop` – The baseline period preceding the trial, default: -100 to 0
`noisestart/noisestop` – Noise preceding the trial, for the covariance, default: -300 to 0
`noiasebasestart/noisebasetop` – Baseline period for the noise, default: -300 to 0

plv – this is a substructure with variables pertaining to phase locking analysis
    dir – The directory containing the PLV trials and results, default: <basedir>/PLV.
    frequencies – List of the frequencies PLV is being done in.
    flag – A temporary flag to indicated whether or not PLV analysis is being done, defunct.
granger – this is a substructure with variables pertaining to Granger analysis
    dir – The directory containing the Granger data, default: <basedir>/Granger.
    model_order – The number of time lags for the Kalman filter, default: 5
    W_gain – An adjustable variable for the Kalman filter, default: 0.5
    N_comp – The number of iterations for the null hypothesis training, default: 0.5
    plv_freq – The frequency used if incorporating PLV in the granger ROIs, default: 0.5
    srcs – String pattern to match Granger-causality causing regions to
    snks – String pattern to match Granger-causality receiving regions to.
    singlesubject – An adjustable flag for the Granger analysis, default: 0 (False)

Subject

blocks – The list of successful blocks the subject has. Default is the list of all from the study.
mri – This is a substructure with variables pertaining to the cortical analysis.
    rawdir – The directory to contain the raw MRI recordings, default
        <study.mri.rawdir>/<subject.name>.
    sourcedir – The folder that the MRI recordings originate from
    first_mpragefile – The first (or only) file that the T1 MPRAGE MRI scan is located.
    dir – The directory with the Freesurfer reconstructions, default
        <study.mri.dir>/<subject.name>.
    corfile – The file with the MEG-MRI coregistration
    ico – The density of the decimated vertices. Default: 7
meg – his is a substructure with more variables pertaining to the MEG recordings
    raid – The MEG RAID server the subject's data is hosted on.
    dir – The directory containing the MEG recordings and MNE results,
        <study.meg.dir>/<subject.name>.
    sourcedir – The directory the MEG recordings were copied from.
    bad_eeg – list of the numbers designations of the bad EEG channels.
    bad_meg – list of the numbers designations of the bad MEG channels.
    sample_rate – The sample rate of the MEG recordings for the subject.
    projfile – The .fif file containing the EOG projections, declared in the analysis stage.
    behav – A structure containing custom behavioral data, made while processing events.
mne – timing and specific constraints for constructing the sensor to cortex mapping
    dir – The directory containing study MNE files. Default:
        <study.mne.dir>/<subject.name>
    avefile – The file with primary condition sensor averages.
    covfile – The covariance file used in the MNE inverse model.
    fwdfile – The file containing the forward model, mapping cortex to sensor activity.
    invfile – The file containing the inverse model, mapping sensor to cortex activity.
plv – this is a substructure with variables pertaining to phase locking analysis
    sample_rate – Defunct.
    sample_times – The times for each sample relative to the trial onset.

Condition

level – Numeric assignment to which level the condition is on. 1 means primary – should be used in constructing the inverse solution, 2 means secondary – distinct set of trials to generate source timecourses, 3 is a placeholder and may be implemented to mean tertiary – a time subset of a secondary trial.

event – This is a substructure with variables pertaining to determining the evoked period

desc – A description of the event if not the condition name itself. Saved in -ave.fif file during the MNE/average_waves function.

code – The numeric codes corresponding the grouped event numbers to this condition.

There are 6 more parameters in pairs that mark time boundaries relative to the onset of the trial events in milliseconds. They are based on the study's times.

start/stop – The trial envelope, default: -300 to 1200

focusstart/focusstop – The most important part of the trial for analysis, default: 100 to 400

basestart/basestop – The baseline period preceding the trial, default: -100 to 0

cortex – This is a substructure with variables pertaining to cortical estimates

brain – The cortical service the condition is meant for, usually average but it may be subject relevant.

plvrefdir – The location to where the average PLV reference label(s) are located. Default: <study.plv.dir>/rois/<condition.name>.

roidir – Old way to organize ROIs, this is a pointer to the ROI directory.

roiset – This new way expects the ROI labels (and data .mat file) to be in the <study.granger.dir>/rois/<condition.cortex.roiset>. This change was made when it was apparently that more conditions may be pointed to the same set of regions. The default is just the condition name.

granger – This is a substructure with variables relevant to Granger analysis.

subsets – Divisions in time for the Granger analysis if relevant. Otherwise empty.

The next three parameters are pointers to files for the Granger processing. Right now gps_filename.m or gpsa_granger_filename.m will automatically determine the Granger filenames so these parameters are not used.

input – The file with the collection of ROI timecourses for input to Granger analysis.

output – The file with the results of the Granger analysis.

signif – The file with Granger null hypotheses for significance testing.