FRIEND

FUNCTIONAL REAL-TIME INTERACTIVE ENDOGENOUS NEUROMODULATION AND DECODING

MANUAL

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D'Or Institute for Research and Education (IDOR)

Neuroinformatics Workgroup

http://idor.org

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1. INTRODUCTION

In Philip K. Dick's science fiction book *Do Androids dream of electric sheep?,* and in the *noir* movie inspired by it, Blade Runner from Ridley Scott, bounty hunters are hired to track down and "retire" biologically engineered androids ("replicants"). They could only be distinguished from "real humans" by decoding subtle empathy-related responses, captured by a special diagnostic device while the examiner probes the subject with emotional scenarios (the "Voight-Kampff test"). Current MRI technology, computer processing and improved algorithms have met with a tremendous advance in our understanding of the neurophysiology of complex emotional and psychological states, making it potentially feasible to decode one's psychological or cognitive states, including complex emotions. Beyond that, the concept of the "Penfield Mood Organ", a device used by characters in the same book to induce specific psychological states through some unspecified brain stimulation technology, does not sound like a very distant reality anymore: transcranial magnetic stimulation, electroencephalography (EEG) neurofeedback and, more recently, functional magnetic resonance imaging (fMRI) neurofeedback bring the possibility of modulating neural states associated with specific psychological states a tenable one. In short, "brain decoding" and "neuromodulation" have come of age.

During the last few years, pioneering research on real-time fMRI-based neurofeedback started to make it into the main specialized scientific journals. Nevertheless, such tools are still mostly out of the reach of the general neuroscience investigator. Instead, a few labs have developed their own computer codes and pipelines, using diverse strategies, which are not easily implementable or reproducible by other groups. Our goal here is to describe a new software tool, the Functional Real-Time Interactive Endogenous Neuromodulation and Decoding (FRIEND) system, which was developed having the basic and clinical investigator of neurofeedback in mind. This tool was developed to be fully compatible and integrated with the Oxford Centre for Functional MRI of the Brain Software Library (FMRIB FSL) suite.

Conceptually, our starting point is that people can be taught to control their own neural activity when they are given feedback that provides information about ongoing neural activity. Initial neurofeedback experiments relied on EEG to estimate neural activity (Colben and Evans, 2011), in which subjects are expected to increase amplitutes in certain frequency ranges (alpha and beta, in general). More recently, the possibility of using functional Magnetic Resonance Image (fMRI) data, which provides increased spatial accuracy at the expense of temporal resolution, was demonstrated for neurofeedback training (Weiskopf et al., 2004; Posse et al., 2002; Sitaram et al., 2010; deCharms et al., 2005). Using this technique, healthy people may improve their cognitive and perceptual abilities while manipulating their own brain states and patients with neurological and psychiatric conditions can learn to control their own brain activation in selected regions or networks of areas.

The FRIEND software includes modules for real time fMRI data processing, univariate (based on prespecified regions of interest: ROI-based) and multivariate (support vector machines: SVM) data classification, as well as a visual feedback tool based on data classification (i.e., neurofeedback). The software thus allows participants to use their own brain signals to increase performance in virtually any kind of behavioral (e.g., motor imagery) or emotional tasks (e.g., increase positive emotions) based on objective neural parameters (brain decoding).

FRIEND was developed and is continuously updated by the Neuroinformatics Workgroup of the D'Or Institute for Research and Education (IDOR), a multidisciplinary team of neuroscientists and neuroinformatics experts:

Core team: Rodrigo Basilio , João Ricardo Sato, Griselda Garrido, Jorge Moll.

Other contributors: Ivanei Edson Bramati, Bruno R. Melo, Patricia Bado, Theo Martins, Fernando F. Paiva, Fabricio Pamplona, Roland Zahn, Fernanda Tovar-Moll.

2. TIPS TO READ THIS MANUAL

The manual is plenty of internal and external (web) hyperlinks to ease swift access to specific subjects of interest. Each entry on the table of contents index is an hyperlink. To return to the last used hyperlink within the text, press *Alt+Left.* Another way is to insert a *Back* button in the Quick Access toolbar. To accomplish this, click the right mouse button on the Microsoft® Office Access Toolbar (Figure 1) and select the *Customize* link. Select *Commands Not in the Ribbon* from the drop-down menu. Double-click the *Back* button in the list to insert it on the Quick Access toolbar. Click *OK* (http://www.pcmag.com/article2/0,2817,2341069,00.asp). Table 1 shows the notation for files and FRIEND interface buttons used throughout this text.

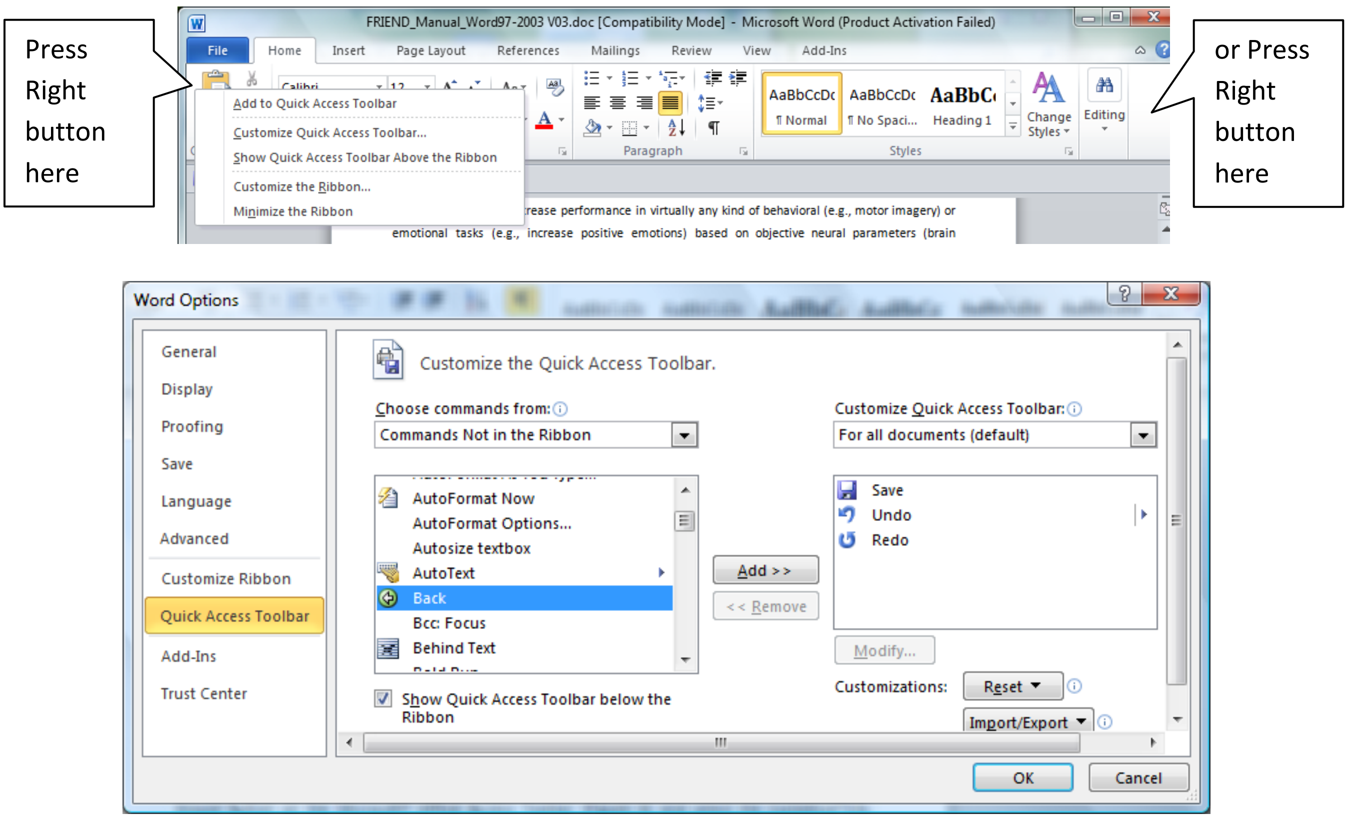

Figure 1. To customise the *Quick Access Toolbar* press the mouse right button as indicated on the top of the figure. Then select *Commands Not in the Ribbon* / *Back* / *Add* / *OK*.

Table 1. Name notation used in this manual

Name in the text	Examples	Description
<RAI>.nii	RAI.nii, MooreMRI.nii	Names within angle brackets (< and >) indicate a placeholder for a value.
project.txt	project.txt	Exact names are referenced plainly
confounds_<crs>.txt	confounds_001.txt	In this example, the <crs> placeholder indicates the current run suffix of the software execution.
Training		FRIEND window buttons are indicated in italic

3. COPYRIGHT AND SOFTWARE REGISTRATION

The FRIEND software was developed at Cognitive and Behavioral Neuroscience Unit and Neuroinformatics Workgroup, D'Or Institute for Research and Education (IDOR, http://www.idor.org) – R. Diniz Cordeiro, 30, 22281-100, Rio de Janeiro, Brazil, Rio de Janeiro, Brazil. Registration of the software at the Brazilian agency of patents and trademarks, *Instituto Nacional da Propriedade Industrial* (INPI – http://www.inpi.gov.br), is waiting confirmation under request number 137820. FRIEND's license is open source and free for non-commercial use. It was based on the FSL license and thus follows similar permissions and restrictions.

4. LICENSE

FRIEND – Functional Real-Time Interactive Endogenous Neuromodulation and Decoding, Release 1.2 (c) 2012, D'Or Institute of Research and Education, Rede D´Or, Rio de Janeiro, Brazil (the "Software").

The Software remains the property of the D´Or Institute of Research and Education ("the Institute").

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5. THIRD-PARTY TOOLS USED TO DEVELOP THE SOFTWARE

The design of the FRIEND software currently includes elements from the FMRIB-FSL and libSVM libraries, both freely available and with stable releases that are being used extensively by the scientific community.

5.1. Windows® FSL library

The FMRIB-FSL, http://www.fmrib.ox.ac.uk/fsl/) is a comprehensive library of analysis tools for fMRI, MRI and DTI (diffusion tensor imaging) brain imaging data developed for Linux/Unix platforms. FSL is written mainly by members of the Analysis Group, FMRIB, Oxford, UK. In the present work, a subset of FSL functions was used to create a Windows® library as described in Appendix fsl commands. Functions in the domain of image processing are: coregistration of images from the same and different modalities, data resampling, Gaussian filtering and skull stripping. Functions implementing the General Linear Model (GLM) and Student *t*-tests were used to obtain data statistics that were used to feed the SVM routines within the FRIEND software.

5.2. Implementation of brain decoding using support vector machines

Features obtained with the statitiscal functions in the FSL Windows® Library are input data to a brain decoding system using the libSVM library developed at the Computer Science and Information Engineering, National Taiwan University. The package includes a multi-class support vector machine module to identify and classify different activation patterns related to distinct cognitive states. The library used in FRIEND is a modified version that includes the bidirectional transformation between bidimensional images (Analyze and NIfTI format files) and vector input structures.

The main idea behind the SVM methodology is to determine a mapping from input data to output class. Once this function is estimated, it can be used to obtain predictions of the classes of new observations based on their input data. In this case, the input data is the normalized BOLD signal intensity of voxels located at the regions specified by the Student t-test volumes generated and thresholded at a cut-off defined by the user. Output data are the different experimental conditions (e.g.: POSITIVE, NEGATIVE). Only the linear kernel SVM methodology is available in the FRIEND software. Although the classification is based on categorical output data, linear SVM can provide the distance of a new observation to the separating hyperplane, the classification boundary between conditions (Figure 2).

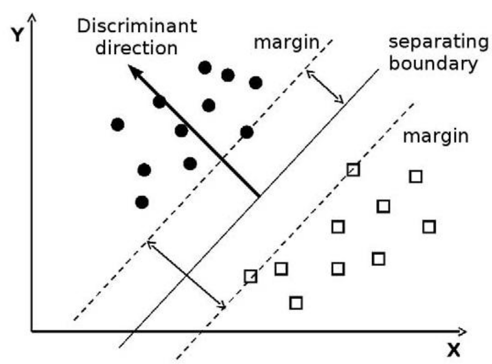


Figure 2 •. The classification boundary is determined by the discrimination line between conditions.

6. EXPERIMENT WORKFLOW OVERVIEW

FRIEND is a Microsoft Windows® software for real-time fMRI processing which includes image processing, statistics and the visualization of brain activation maps with neurofeedback for training and classification of cognitive states. Figure 3 shows the FRIEND interfaces (A and B panels), some examples of cognitive states as presented to the participant (C). Optionally, feedback figures associated either with real or sham feedback, can be continuously presented to the participant (D). Figure 6 shows the example of a ring, but any other figure could be used. The distortion of the ring, in a real feedback experiment, will change according to the SVM classification of the cognitive state of the subject. Only one cognitive and one neurofeedback figure are shown at a given time to the participant while performing the experiment. One anatomical and one functional volume must be acquired offline to be used as reference images.

Functional images must be obtained afterwards and during real-time acquisition. The experimental design is described in a design file while other parameters are entered through the software interface window. The software GUI displays a control window where motion correction of functional images to the reference brains is displayed in graphic form (B). Data statistics is accomplished using resources as the General Linear Model (GLM), Student *t*-tests and SVM classification routines. The rate of “success” (correct classification or prediction) is updated continuously in the same window (B).

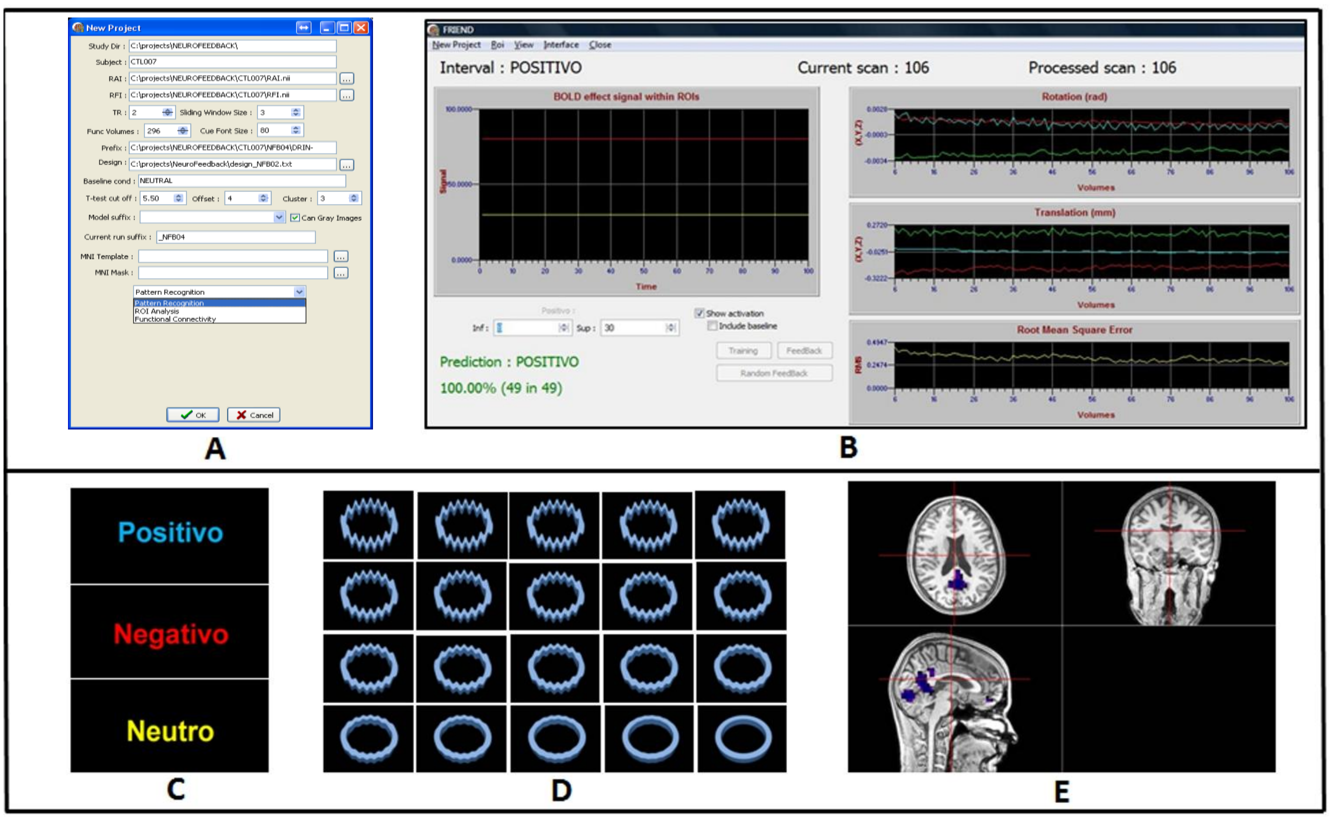


Figure 3 •. A simplified overview of the software environment.

7. FRIEND SOFTWARE

7.1. System requirements, download and installation

The FRIEND software can be executed on the Windows® XP and Vista operating systems. A high-end computer workstation is recommended (by e.g. 4-dual core, 1.7 MhZ, 6 GB RAM) to be compatible with real-time execution. FRIEND programming is not parallel, but multithreading was implemented and will be useful on multiple core computers. All steps of image registration, motion correction, feature selection (which can be based on support vector machines [SVM] or general linear model [GLM] "functional localizers", or on a priori ROIs) and SVM classification can generally be performed within a TR of 1.5 second or less (single-shot EPI, 64x64 to 80x80 matrix, 22-37 slices), a period of time compatible with the acquisition of one fMRI volume. Microsoft .NET 3.5 or superior must be installed.

The software can be downloaded from the FMRIB Oxford website (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/OtherSoftware) or directly from its repository (http://idor.org/neuroinformatics/friend). If you are using FRIEND in your research, please cite the download links above and the reference paper:

Sato JR, Basilio R, Paiva FF, Garrido GJ, Bramati IE, Bado PP, Tovar-Moll F, Zahn R, Moll J. Real-time fMRI pattern decoding and neurofeedback using FRIEND: an FSL-integrated BCI toolbox PLOS One, accepted (2013).

Clicking on the FRIEND.exe file will open the software interface. This manual can be used as a guide to execute the software. However, at some point, it will be more useful as a reference guide as a dynamic set of videos showing software usage and functionalities is under preparation and will be available on a youtube channel soon.

7.2. Software functionalities

There are three main execution options in FRIEND: (1) Multivoxel pattern decoding, (2) ROI Analysis and (3) Functional connectivity. FRIEND provides the user with great flexibility as each option can can be executed with different options, depending on the applicability: with or without neurofeedback, training or feedback, standard or user-provided templates and ROIs, etc. Figure 4 shows the pipeline for the three options in detail.

			1 Training	1 Classification	2 BOLD	3 Correlation
Input		Acquisition of anatomical and functional images of reference	● (green)	● (blue)	● (blue)	● (blue)
		Configuration of input parameters[1]	● (green)	● (blue)	● (blue)	● (blue)
Image processing		Acquisition of real-time functional images	● (green)	● (blue)	● (blue)	● (blue)
		Coregistration and skull stripping of reference images using FSL	● (red)	● (blue)	● (blue)	● (blue)
		Spatial and temporal processing of functional images	● (red)	● (blue)	● (blue)	● (blue)
Statistics		fMRI data statistics (GLM maps) and features extraction using FSL	● (red)	● (blue)	● (blue)	● (blue)
		Training of classifier with libSVM library	● (red)			
		Mean ROI(s) BOLD extraction from preprocessed images			● (blue)	● (blue)
		ROI(s) correlations				● (blue)
		Brain state scoring based on projections from trained SVM		● (blue)		
Feedback to	Participant	User task instructions	● (red)	● (blue)	● (blue)	● (blue)
		Neurofeedback figures[2]		● (blue)	● (blue)	● (blue)
	Researcher	User task instructions	● (red)	● (blue)	● (blue)	● (blue)
		Neurofeedback figures[2], radar-plot		● (blue)	● (blue)	● (blue)
		Head motion estimates	● (red)	● (blue)	● (blue)	● (blue)
		Activation maps	● (red)	● (blue)	● (blue)	● (blue)
		Classification accuracy		● (blue)		

● (green): offline/real-time processing, ● (red): offline, ● (blue): real-time

[1] Study directory, type of classification, brain reference images, number of volumes, TR, statistical thresholds, etc.

[2] Figures from software distribution (thermometer, ring) or provided by user

Figure 4. Flowchart of three FRIEND processing pipelines for neurofeedback: 1: Support Vector Machine based neurofeedback, defined on the basis of projected values onto the discriminative hyperplane ; 2: BOLD level real-time display from pre-defined ROIs; 3: Real-time functional connectivity neurofeedback based on the correlation between the signals from different ROIs.

7.2.1. Multivoxel pattern decoding - Training the SVM classifier

SVM has an intrinsic abili SVM is its intrinsic ability to deal with the typical fMRI datasets, which contain typically tens of thousands voxels, i.e., when the number of features far exceed the number of measurements.

Ultimately, the goal of machine learning methods applied to fMRI data is to maximize the ability to make predictions new, unobserved data, i.e., to allow generalization from observed data ("training") to new datasets (Vapnik 1998; Bishop 2006).

In FRIEND's control window, when the "training" checkbox is selected, the SVM classifier will be initially trained with brain activation patterns associated with the specified conditions of interest in the training fMRI dataset. In addition, in order to increase the signal to noise-ratio, each example is built by computing an average volume among three (or another user-defined number) previous volumes (sliding window average).

The main concept behind the two-class SVM methodology is to determine a mapping from input data (activation pattern) to output experimental condition. Once this function is estimated, it can be used to obtain scores for predictions of the classes of new observations based on their input data (Mourão-Miranda et al. 2005; Sato et al. 2008). The input data is the normalized BOLD signal intensity of input voxels. Currently, only the linear kernel SVM method is implemented in FRIEND.

The brain voxels of a scan are first mapped into an input vector $\boldsymbol{x}$, and this vector is then labeled according to the respective experimental condition when this scan was acquired. In the following, these set of input vectors and labels are considered as the training data in SVM. After training the SVM, the projection of a new fMRI image volume on the discriminating hyperplane is given by $(\boldsymbol{x}^T\boldsymbol{w} + b)$, where $\boldsymbol{w}$ is a vector containing the hyperplane coefficients and b is a constant.

7.2.1.1. Multivoxel pattern decoding - Real time classification

After training a SVM on the initial dataset, predictions about the current cognitive/neural state of the subject can be made in real time based on incoming fMRI image volumes. At this stage, neurofeedback-based modulation is accomplished through the presentation of visual feedback stimuli that are contingent on SVM classification. Although the classification is based on categorical output data, linear SVM can provide the distance of a new observation to the separating hyperplane, the classification boundary between conditions (Sato et al. 2008); this projection ("decision value") is then used for the neurofeedback display. In other words, the relative position of the input data projection to the classification boundary at discriminative hyperplane is the measure that will define which figure (from a bitmap-grid stimuli set) will be displayed as a proxy of the underlying cognitive state of the participant. Further information about real-time classification/projection can be found in (Mourão-Miranda et al. 2005; LaConte et al. 2007; Sato et al. 2008; LaConte 2011).

7.2.2. ROI Analysis

The real time preprocessing module includes options for univariate (ROI-based) and multivariate (SVM) data analysis (Sato, Fujita, et al. 2009; Haxby 2012) and/or classification, coupled with a visual neurofeedback module. This enables participants to use their own local (single ROI or combined ROIs) or distributed brain signals (correlation among ROIs or multivoxel pattern-based brain decoding using SVM) to modulate performance in a wide range of behavioral (e.g., motor task), cognitive (e.g., motor imagery) or emotional tasks (e.g., basic or social emotions).

When employing multivoxel pattern brain decoding (SVM), a first “training session” (i.e., a non-online “functional localizer”) is required (LaConte 2011; Sitaram et al. 2011). This initial data is used to train the classifier to discriminate between the experimental conditions of interest (currently, a two-class SVM classifier is implemented, but multiclass SVM is also feasible). The trained SVM is then used in the subsequent brain decoding sessions (testing sessions), in which the subjects will engage in the same conditions of interest. To allow for controlled studies, FRIEND offers the option of running an experiment with or without contingent neurofeedback (depending on assignment of the participant to the neurofeedback or to the non-feedback /sham group). In its current implementation, FRIEND requires at least one condition of no interest (i.e., baseline), which should be included between blocks of the main experimental conditions, in order to allow for online signal normalization and detrending.

7.2.3. Functional localizers and feature selection

When using ROI or SVM-based neurofeedback, users may opt for running a General Linear Model (GLM)-based statistics (M. Woolrich et al. 2001) on the initial dataset (e.g., first functional run) to be used as a functional localizer for single-region neurofeedback, for dual-region correlation analysis or before SVM training. This step employs embedded routines from the FSL library (*feat_model* and *fsl_glm*), allowing for *a priori*-defined statistical contrasts, which can be used for optional feature selection/masking of relevant voxels identified at functional localizer or training session (see p.164-165 (Poldrack et al. 2011). This is an important step due to the following reasons: (i) for single ROI neurofeedback or dual-ROI real-time correlation, using a percentage of the more active voxels within selected anatomical ROIs can better accommodate individual differences; (ii) whole brain classification analysis leads to high dimensionality of the data, including confounders and irrelevant variables, so a feature selection step helps reducing dimensionality; and (iii) these procedures minimize the possibility that artifactual or uninformative voxels influence the results.

7.2.3.1. ROI-based neurofeedback

In the case of model-driven experiments, FRIEND allows the use of ROIs not only for real time visualization of online brain activity but also for ROI-based BOLD neurofeedback. The GUI allows selecting ROIs from standard atlases (MNI, AAL, etc), from a mask file or by manually selecting activation clusters from GLM analysis of a functional localizer scan, which can be saved as ROIs for subsequent use. In the latter case, a moving-average BOLD signal from these regions can then be displayed (e.g., as a thermometer, a moving ring, a radar chart). As shown in several previous studies, subjects can modulate BOLD activity of specific ROIs, guided by neurofeedback signals (Caria et al. 2007; deCharms et al. 2005; Zotev et al. 2011). The basic concept is to use a block-design paradigm in which participants are instructed to try to increase or decrease BOLD signal averaged within an ROI, with the aid of a feedback display (see Supplementary video 1). Furthermore, the ROI approach can also be employed for real-time classification, as an SVM can be trained by considering the moving-average signals from *n* pre-selected regions as input variables. Thus, SVM can be used to create a single feedback representing the cognitive state of the subject by considering the multivariate representation of several pre-selected ROIs.

7.2.3.2. Functional connectivity

FRIEND also allows a functional connectivity-based neurofeedback using a sliding window, Pearson correlation coefficient method. This approach enables experiments probing the effects of endogenous modulation of the connectivity between user-defined ROIs (including cortico-subcortical connectivity that cannot be assessed using non-invasive EEG-based methods). At each new volume acquisition, the coefficient is iteratively calculated over the last w scans (a user-defined parameter). To accomplish this, the mean intensity $\overline{roi}_t = \sum_{j=1:m} x_j / m$ is calculated over the m voxels of the ROI, roi, at each time point t for subsequent calculation of the ROI mean $\overline{roi} = \sum_{t=1:w} \overline{roi}_t / w$. Thus, for ROIs A and B, the Pearson coefficient over a w-sliding window at time t is:

$$\rho(A,B)_t = \frac{\sum_{k=1:w}(\bar{A}_{t-k} - \bar{A})(\bar{B}_t - \bar{B})}{\sqrt{\sum_{k=1:w}(\bar{A}_{t-k} - \bar{A})}\sqrt{\sum_{k=1:w}(\bar{B}_{t-k} - \bar{B})}}$$

Our pilot studies have shown that more stable values of ρ are obtained with w=[10..15]. This real-time functional connectivity measure can then be displayed as a feedback to the participant by using a time-series plot or user-defined visual pattern (e.g., a thermometer). The mean value of the time-varying correlation scale (used to set the midline value of the feedback thermometer) employs a sigmoid-weighting discounting function, which provides estimates that are more influenced by more recent values, relative to older ones (again, this weighting function can be set by the user, but our experience suggest that a value of 10 volumes is adequate). The upper and lower bounds of the correlation scale (which define the top and bottom levels of the thermometer) are defined on the basis of the calculated standard deviation (generally 1-1.5 s.d.) of the mean over the *n* last volumes. This provides a smooth and flexible control of the feedback thermometer feedback, and a more "natural" experience for participants whilst they attempt to modulate their own ROI-based correlations.

8. SETTING A REAL-TIME EXPERIMENT WITH AND WITHOUT NEUROFEEDBACK

Directory structure (directories in green)	Examples (directories in green)	
<study1>	**NEUROFEEDBACK**	study directory where data for all participants will be stored.
<subject1>	**CTL0007**	Is the subject directory where data from the execution of an experiment for a specific participant will be saved (e.g.: Subject01). If more than one session is run for the same subject, it is advisable to create one subject directory for each session (e.g.: Subject01_sess1, Subject01_sess2). Otherwise, some intermediate files generated by FRIEND will be rewritten on each session execution.
states	**states**	A directory containing the stimulus condition figures (Figure 5) that will be presented to the participant. If not present, the States directory from the FRIEND root directory will be used. The user has the option of automatically creating stimulus condition figures defined through a text file. Figures defined in this manner take precedence over figures inside any states directory. Directory containing figures indicating the cognitive state

		that must be elicited by the participant. There will be one filename for each condition in the design text file. Standard format files are recognized by the software (e.g: jpg, tif, png). If the directory doesn't exist in the subject directory, the States directory from the FRIEND root directory will be used.
<design>.txt	design_NFB01.txt: 1-20, NEUTRAL 21-30, PRIDE 31-40, NEUTRAL …..	A text file containing the study design with the conditions of the experiment must be created. More than one file can be created as each run in the session can have a different design. Each line in the file contains the interval of scans associated to the condition that will be presented.
<RAI>.nii <RFI>.nii	CTL0007_MRI.nii CTL0007_EPI.nii	A single high-resolution brain volume and a single low-resolution brain volume, heretofore named as "Reference Anatomical Image" (RAI) and "Reference Functional Image" (RFI) respectively need to be acquired on a first-basis, i.e., before the FRIEND program is executed and before acquisition of the functional scans. Both RAI and RFI should be in approximate coregistration, something that can be easily implemented as these scans are acquired in the same session. Once the reference images were acquired and the interface window was configured, real-time execution begins. The real-time functional images (RTFI) acquired subsequently must have the same acquisition parameters as RFI.

A sequence of steps for the execution of FRIEND is provided in this section. For the sake of clarity, some specifics details regarding input and output files were omitted on this flow description. However, a thorough description can be found on Table 4. Examples of these files are provided on the appendixes. Deviations from the sequence here provided would be expected as each center can customise its own workflow depending on the type of experiment performed, the user-interface communication system (visual, auditive) and organizational issues.

8.1. Stimulis conditions

Visual stimuli can be provided in three ways. FRIEND searches displays visual stimuli according to the following order of precedence:

1. Figures defined through a text file that are created automatically by FRIEND.

2. Figures in the states directory that is inside the subject directory.

3. Figures in the states directory that is inside the FRIEND directory.

Currently, only figures in jpeg file format are allowed. Figure 5 is an example of stimulus conditions presented as text, where each colour is associated with a specific condition (eg.: yellow is neutral, red is anger and blue is).

Figure 5. In this example, visual stimuli containing keywords for the participant to recall real life autobiographical events are shown. Emotional valence is associated with the color of words: yellow for neutral, red for negative and blue for positive.

8.2. Neurofeedback figures

By default, a set of figures is provided with the distribution of the software (Figure 6) to be used in association with the SVM output. However, the user can employ customized images of any sort (by e.g.: rectangles, circles, etc). Currently, only the JPEG format is allowed. Work with other tandard picture formats (GIF, TIFF, JPEG, etc) is on progress. Observe that, as will be described in more detail below, the figures can be displayed in a random mode, i.e. with no connection to the SVM output.

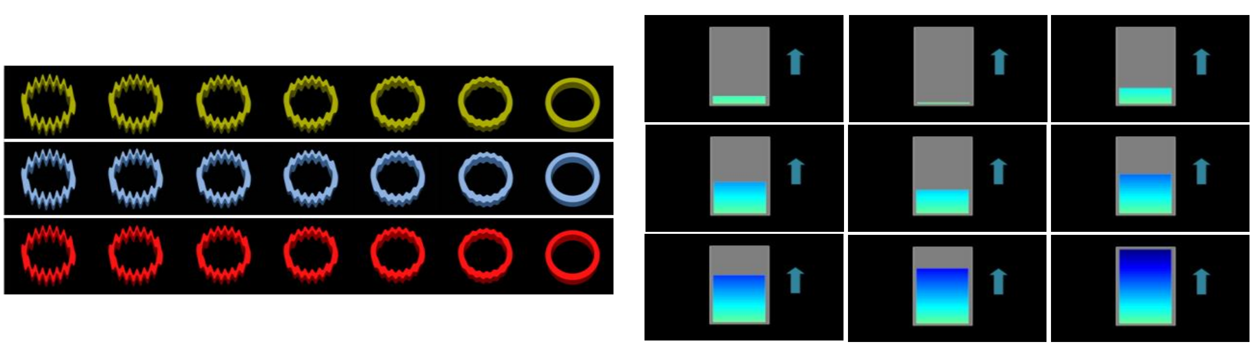


Figure 6 •. Left: the distortion of the ring displayed as neurofeedback provides the participant with a visual feedback that can be directly correlated or randomically associated with the underlying cognitive state of the participant. Right: another option is the utilization of a thermometer where higher levels are associated with higher direct correlation.

8.3. Hardware setup

Video setup: Select the Windows® Properties configuration that better adapts to your experiment. By e.g. Open NVIDIA Settings on Windows® desktop and select “Configured independently from each other (Dualview)” (Windows® XP: .

Trigger availability: If a trigger system is available, check that the TTL pulse from the fMRI scanner is being received by the computer where FRIEND is running.

Real-time data exporting: For execution, data must be transferred in real-time to a working directory in the computer where FRIEND is run. FRIEND was extensively tested using a Philips® Achieva scanner (software version 2.6.3) using the Philips® DRIN-dumper software provided under a clinical science agreement. This program exports data to the workstation were FRIEND is run as soon as fMRI data is available. Tests with real-time Siemens® data (Espree scanner, software version VB17) is underway. Users should refer to the manufacturer of the scanner of their environment for assistance as proprietary software for data transfer might be necessary.

8.4. FRIEND execution

Once the required directory structure and hardware is configured, the FRIEND.exe program can be executed. The processing sequence is described below.

1. **Input window parameters**: Before effectively starting the experiment, the FRIEND interface window (Figure 7) must be filled in with the parameters necessary for the execution of the experiment. A detailed description of the fields can be found on Table 2.

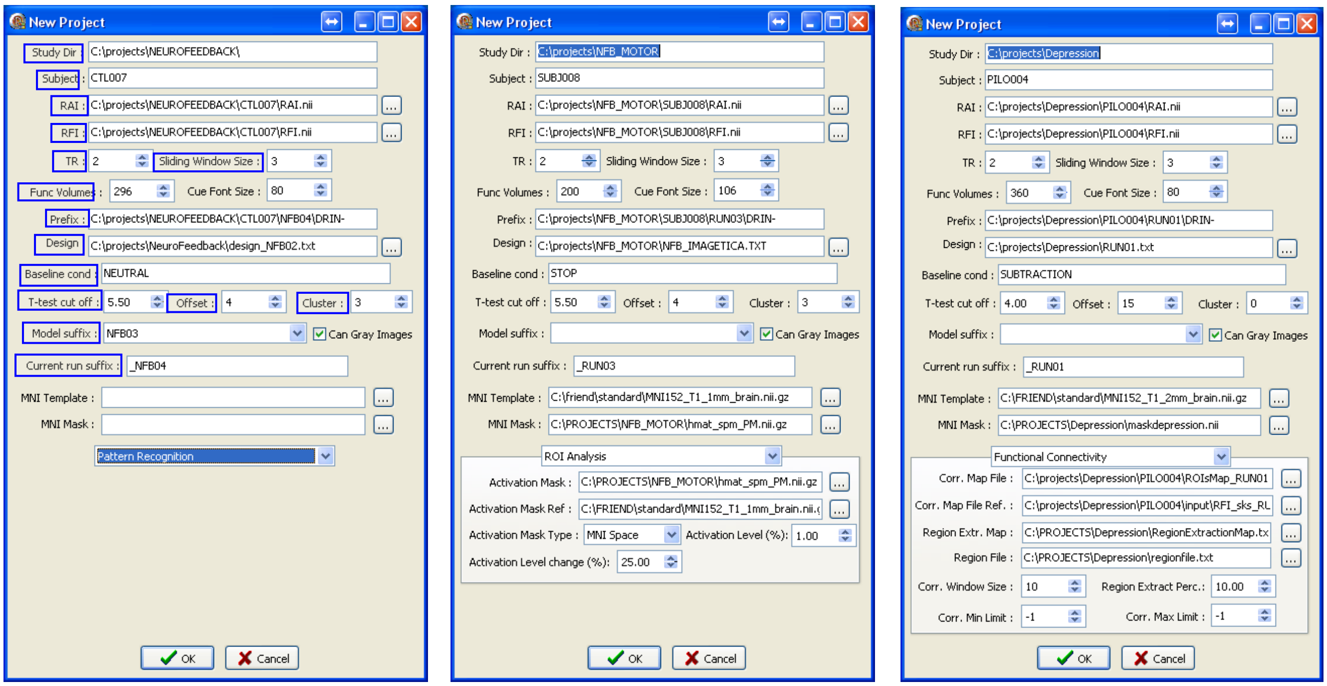


Figure 7 •. FRIEND interface for the entry of study, subject and processing parameters from the top to the middle of the window. The remaining of the window shows context-sensitive menus according to the type of processing (Pattern Recognition, ROI Analysis, Functional Connectivity). The blue boxes are hyperlinks to the location where the fields are explained.

Table 2 •. Description of input parameters for the execution of the FRIEND software.

Field name	Description
Study dir	<study> • is the parent working directory (e.g: c:\neurofeedback\study\). The directory must exist before beginning the execution of FRIEND.
Subject	<subject> • is the subject identifier directory (e.g. CTL0001) and a

	subdirectory of <study>. Required data for the execution of FRIEND is required in the “Required directory structure and files for FRIEND execution” section. Study parameters and all files generated during FRIEND execution will be saved under this directory.
RAI	Directory path and name of the Reference Anatomical Image (<RAI>.nii •): <study>\<subject>\<RAI>.nii. The high resolution image must be acquired before running FRIEND and installed in the <subject> directory.
RFI	Directory path and name of the reference functional image (<RFI>.nii •): <study>\<subject>\<RFI>.nii. The functional image must be acquired before running FRIEND and installed and installed in the <subject> directory. Ideally, both images <RAI>.nii, and <RFI>.nii should be in raw alignment.
TR	Repetition time of the functional study. •
Sliding window size	<sliding_window_size> • is the number of volumes to be averaged in the sliding window for the creation of the classification input images (<study>\<subject>\4D_mc_ms_G_3sw_*.nii).
Func volumes	<functional_vols> • is the number of volumes acquired during the session of the study.
Prefix	A string of the name of the directory where the functional real-time images (RTFI) are stored and the beginning of the name (<prefix> •) of each file, which is the same for all images. For Philips scanners it could be “c:\data\DRIN-“ as the prefix “DRIN-“ is prepended to the name of acquired images.
Design	Directory path and name (design •) of the text file containing the experimental design of the study.
Baseline cond	<baseline_condition> • is the name of the baseline condition. Must be the same as specified within the design file (e.g. NEUTRAL).
t-test cut off	<cut_off> • is the Student t-test threshold applied to tstats_features_ALL_<crs>.nii file to obtain tstats_features_cut_off_<crs>.nii.
Cluster	<cluster_size> • is the minimum cluster size in tstats_features_cut_off_<crs>.nii that will enter tstats_features_<crs>.nii.
Offset	<offset> • is the number of functional volume images discarded initially (dummy scans) due to the delay of the BOLD effect that is applied during the machine learning phase only. Note that for the General Linear Model (GLM) calculation, a previous step, all volumes are used.
Model run suffix	<mrs> • is the suffix from a previous run that will be used as classifier. The program will display a combo box for selection within a list of existing suffixes. Either individual (e.g.: run01) or paired runs (e.g.: cumulative_run01_run02) can be used. In the latter case, data is concatenated as if it were only one run.
Current run suffix	<crs> • is the suffix added to the name of the files created during the current run (e.g. run1).

2. **Study parameters registration**: After pressing the *OK* button, parameters from the interface input window (Figure 7) will be saved to a text file in the subject root directory. An identical copy will be saved in the FRIEND root directory. The next time FRIEND is executed, default parameters will be read from the file in the subject directory. If the file doesn't exist, parameters from the file in the FRIEND directory will be used.

3. **Skull stripping:** The FSL BET program is used to strip extracerebral tissue from the RFI. The result is automatically displayed in a pop-up window for visual inspection (Figure 8). Skull stripping can be redone iteratively with other parameters (see http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/BET/UserGuide for a detailed description of available options) until the *OK* button is pressed.

4. **Coregistration**: Before starting real-time processing, the first step is coregistration of the RFI to the RAI to create a coregistration matrix. The transformation will be used for motion correction of real-time functional images.

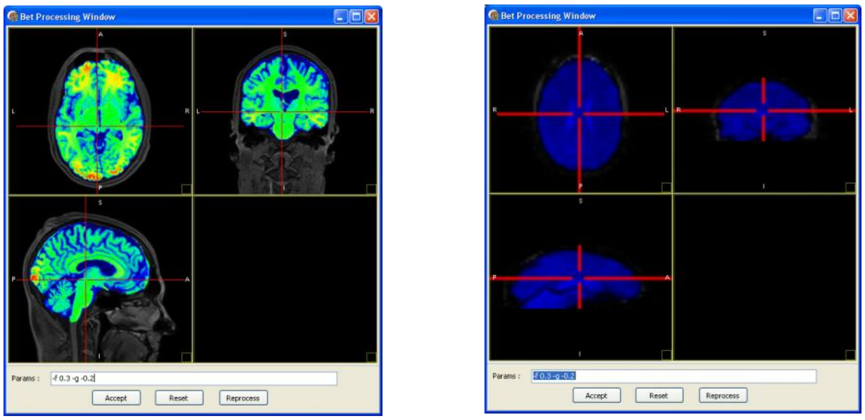


Figure 8. Output of FRIEND Quality Control menu. Left: non-stripped (background) and stripped (overlay) reference anatomical image (RAI). Right: non-stripped (background) and stripped (overlay) reference functional image (RFI).

5. **Real-time processing:** The execution of FRIEND during real-time can be monitored on the control window (Figure 9). Optional windows can be displayed to monitor the display of activation on a low-resolution anatomical image (Figure 10). A detailed description of the parameters required on this window can be found on Table 3. Once the experiment is started and the acquisition of functional images begins, Windows® FSL library routines are executed, including motion correction, Gaussian filtering and coregistration (using the transformation matrix created previously) for real-time display of motion correction parameters.

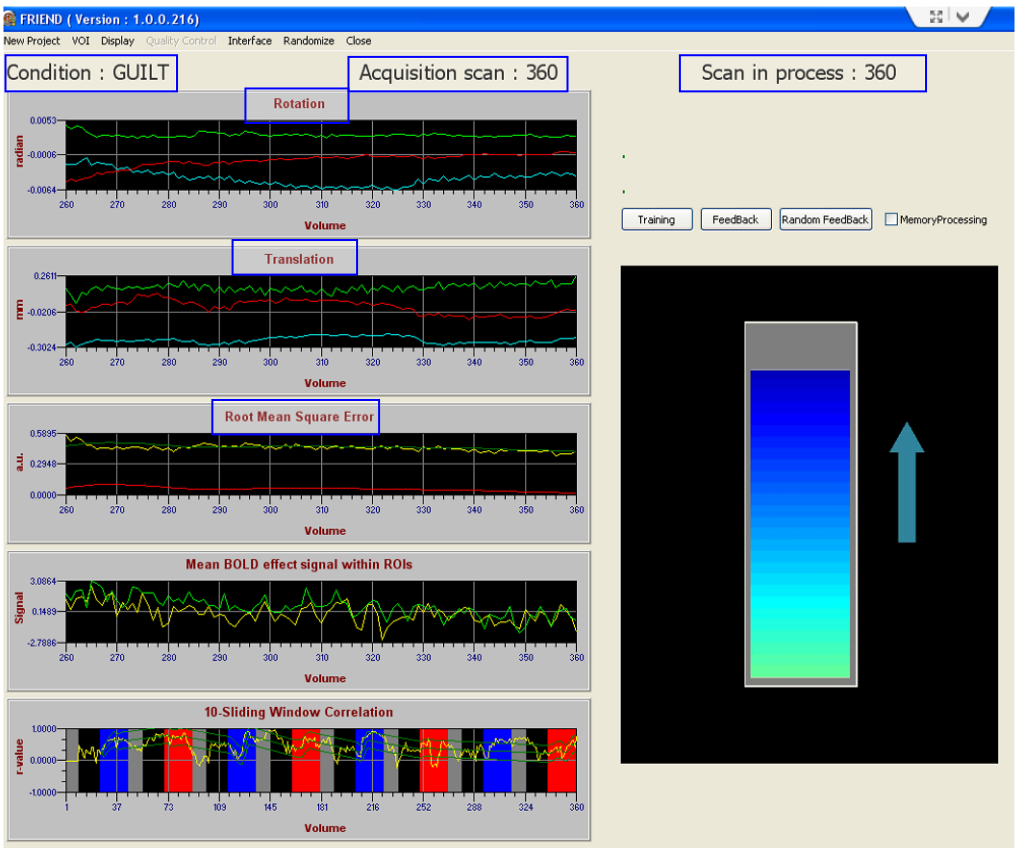


Figure 9 •. Information about motion correction, data training, data classification and intermediate kappa values are displayed. The blue boxes are hyperlinks to the location where the fields are explained.

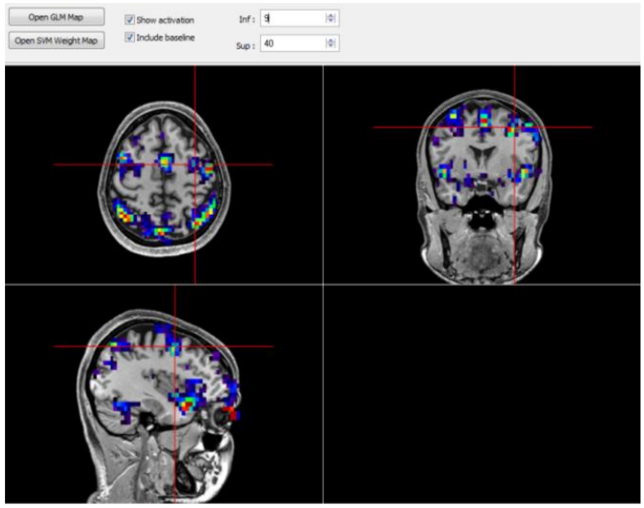


Figure 10 . Low resolution structural image used to display activations in real-time.

Table 3 •. Input parameters for running FRIEND.

Field name	**Description**
Interval •	Current condition block name (e.g. POSITIVE).
Current scan •	Displays the number of the current volume
Processed scan •	Displays the number of the last processed scan
BOLD effect signal within ROIs graph •	The user can draw ROIs within the 3-slices brain view interface. The average BOLD effect signal within the ROIs is shown on the graph.
Rotation (rad) •	Rotation in radians for all acquired functional images to RFI.
Translation (mm) •	Translation in mm of all functional images to RFI.
Root Mean Square Error •	Root mean square error obtained with a FSL routine.
Show activation •	Select to display activation maps (BOLD signal subtracted from previous baseline).
Include baseline •	Default display is only for main conditions, excluding baseline. Select to also show activation during <baseline condition> relative to preceding condition.
Training •	Select if on training phase.
Feedback •	Select if neurofeedback is to be provided to the participant, based on the cognitive state prediction.
Random feedback •	Select if the neurofeedback figures will be displayed with no relation to the current cognitive state prediction.

6. **fMRI data training**: The experiment effectively begins when the *Training* button is pressed. If the training option is selected in the control window, the SVM classifier will initially be trained by brain activation patterns associated with the current condition, derived from the GLM and condition contrasts automatically defined by the program. Voxel intensities from the fMRI images are selected according to its presence on t-test images thresholded by a user-defined parameter (cut-off) or by a user-defined percentage of active voxels, after rank-ordering. In future studies, the training phase could be suppressed depending on availability of normative databases.

7. **fMRI data statistics**: The General Linear Model (GLM) is implemented using the Windows® FSL library, which is used to obtain filtered t-test images based on the condition contrasts defined.

8. **Between-runs configuration**: Subsequent runs (either for training or classification) will demand the modification of some input parameters on the FRIEND interface.

9. **fMRI data classification**: Using information obtained during the training stage, the SVM module makes predictions about the current cognitive state of the subject based on multivoxel pattern decoding. Observe that a new experiment session comprising steps 1-5 must be run for SVM classification. On this phase, user interaction is available through the presentation of neurofeedback figures. If the random option was selected, there will be no relationships among SVM prediction and the feedback figures. If the neurofeedback option was selected, the neurofeedback displayed figures will be shown (Figure 6) according to the weight vector of the SVM output to guide the participant during the experiment. The distance to the hyperplane (Figure 2) is the measure that will define which figure will be displayed as a representation of the underlying multivoxel pattern and associated cognitive state of the participant. If the random option is selected, the neurofeedback output figures are displayed randomly and thus are not related with the underlying cognitive state predicted by the classification module.

10. **Accuracy determination**: The kappa value reflecting the accuracy of the classification is displayed and updated on the interface of the control window at each new functional image acquisition. The associated confusion matrix is stored in a text file at the end of each run of the experiment for future reference.

11. **Post-processing**: Final and intermediate files created are stored for offline processing. Once the entire running is finished, obtained motion parameters can be entered in the GLM model as covariates, and the thresholded output is used for generating the feature maps prior to the SVM training, which is then used to classify the next run.

9. FRIEND SOFTWARE FILES

This section describes the files that come with the distribution, as well as intermediate and final files created through the execution of the software. The reader will note that it contains much more information about files that will usually be found on software manuals, if any. The decision was strategic. Over time, this manual will be updated to be used mainly as a reference guide and hopefully, it will be particularly useful for plugin or toolbox developers. For this reason, this section is still under development. Although the manual can be used to learn the software usage, Youtube videos that are currently under preparation will be more suitable to speed up the learning curve of the software utilization.

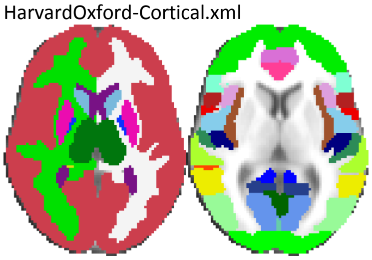
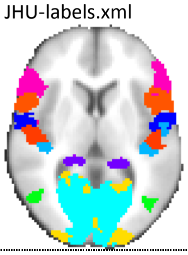
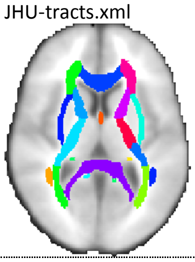
After uncompressing the download file, the FRIEND directory will be created. Contents are described in detail in the following paragraphs.

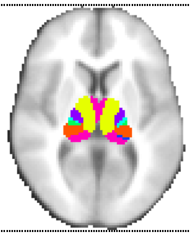
9.1. Directories and files in FRIEND directory

FRIEND	Root FRIEND directory.
atlases	Brain atlases included with FSL: http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Atlases.
HarvardOxford	Probabilistic atlases with 48 cortical and 21 subcortical structural areas.
JHU	White matter atlases.
Juelich	Probabilistic atlas with 52 grey matter structures and 10 white matter structures.
MNI	9 anatomical structural regions.
Talairach	A conversion of the original Talairach structural labellings.
Thalamus	Probabilistic atlases of 7 sub-thalamic regions.
feedback	Repository of user-provided neurofeedback figures
<condition_1>	Directory for feedback figures on condition 1
....	....
<condition_n>	Directory for feedback figures on condition n
flirtsch	The FMRIB's Linear Image Registration Tool is a fully automated robust and accurate tool for linear (affine) intra- and inter-modal brain image registration methodology.
fnirtcnf	The FSL nonlinear registration methodology.
luts	RGB colormap look up tables.
standard	FSL directory with standard templates.
tissuepriors	MNI152 standard space T1-weighted average structural template images.
states	Directory with stimulus figures of cognitive or emotional states.
transferfunction	Transfer function
images	
tissuepriors	
Dicom.dll	DICOM link library.
FRIEND.exe	FRIEND executable.
FriendLauncher.exe	FRIEND launcher.
fsl.css	
fsl.dll	FSL (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/) is a comprehensive library of analysis tools for FMRI, MRI and DTI brain imaging data. fsl.dll is the dynamic link library for Windows® created by IDOR. The original source code was modified : insertedin a dll. Incompatibilites with windows were solved. Most FSL commands can be called through a function (see Appendix A for details)
fslexec32.exe	FSL auxiliary file used to execute a specific GLM processing.
liblinear.dll	LIBLINEAR – a Library for Large Linear Classification (http://www.csie.ntu.edu.tw/~cjlin/liblinear/)
libsvm.dll	LIBSVM is a library for Support Vector Machines (SVMs) (http://www.csie.ntu.edu.tw/~cjlin/libsvm/). libsvm.dll is the Windows® Dynamic Link Library created by IDOR that incorporates the LIBSVM library and routines for reading NIfTI format files and transforming it into a vector matrix, suitable for SVM processing.
sf.dll	Streaming library
study_params.txt	Parameters used during the execution of FRIEND are stored in a text file. They are both user-defined parameters entered through the software interface and other default parameters that can be overridden editing the text file. The study_params.txt file that is in the subject directory has precedence over the one in FRIEND's directory..

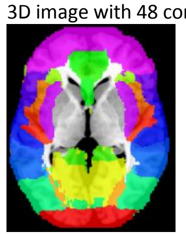
9.2. Files in FRIEND/atlases/

FRIEND/atlases	Information on this section was extracted from:http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Atlases . Many atlases are provided with FSL (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Atlases; http://fsl.fmrib.ox.ac.uk/fsl/fsl4.0/fslview/atlas-descriptions.html). The tool atlasquery is a command-line tool for atlases supplied with FSL, in the same way as is possible via FSLView. It takes as input the name of one of the FSL atlases together with either a coordinate of interest or a mask. The syntax is: atlasquery [-a "<atlasname>"] [-m <maskimage>] [-c <X>,<Y>,<Z>] Compulsory arguments (You MUST set one or more of): -a,--atlas name of atlas to use Optional arguments (You may optionally specify one or more of):

	-V,--verbose switch on diagnostic messages -h,--help display this message -m,--mask a mask image to use during structural lookups -c <X>,<Y>,<Z> mm coordinates of the point of interest --dumpatlases Dump a list of the available atlases
HarvardOxford-Cortical.xml 	The Harvard-Oxford cortical and subcortical structural atlases are probabilistic atlases covering 48 cortical and 21 subcortical structural areas, derived from structural data and segmentations provided by the Harvard Center for Morphometric Analysis. T1-weighted images of 21 healthy male and 16 healthy female subjects (ages 18-50) were individually segmented by the CMA using semi-automated tools developed in-house. The T1-weighted images were affine-registered to MNI152 space using FLIRT (FSL), and the transforms then applied to the individual labels. Finally, these were combined across subjects to form population probability maps for each label.
HarvardOxford-Subcortical.xml	idem
JHU-labels.xml 	The Jülich histological (cyto- and myelo-architectonic) atlas is a p probabilistic atlas created by averaging multi-subject post-mortem cyto- and myelo-architectonic segmentations, performed by the team of Profs Zilles and Amunts at the Research Center Jülich and kindly provided by Simon Eickhoff. The atlas contains 52 grey matter structures and 10 white matter structures. This is an update to the data used in Eickhoff's Anatomy Toolbox v1.5. The atlas is based on the miscroscopic and quantitative histological examination of ten human post-mortem brains. The histological volumes of these brains were 3D reconstructed and spatially normalised into the space of the MNI single subject template to create a probabilistic map of each area. For the FSL version of this atlas, these probabilistic maps were then linearly transformed into MNI152 space.
JHU-tracts.xml 	
Juelich.xml	
MNI.xml 	MNI152 standard-space T1-weighted average structural template image derived from 152 structural images, averaged together after high-dimensional nonlinear registration into the common MNI152 co-ordinate system. It corresponds to the "152 nonlinear 6th generation" atlas
Talairach.xml 	A conversion of the original Talairach structural labellings, provided by Jack Lancaster and Diana Tordesillas Gutiérrez at the Research Imaging Center, UTHSCSA, Texas. This is a digitised version of the original (coarsely sliced) Talairach atlas (Lancaster 2000) after the application of a correcting affine transform (Lancaster 2007) to register it into MNI152 space
Thalamus.xml	The Oxford thalamic connectivity atlas is a probabilistic atlas of 7 sub-thalamic regions, segmented according to their white-matter connectivity to cortical areas, kindly provided by Heidi Johansen-Berg and Timothy Behrens, FMRIB. This connectivity atlas reports probability of anatomical connection from points in the thalamus to each of 7 cortical zones. These probabilties are calculated using probabilistic diffusion tractography in multiple subjects. For more details see the Thalamic Connectivity Atlas web page.

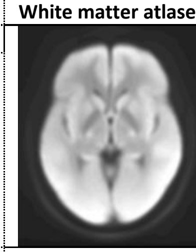
	

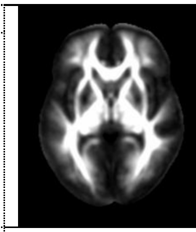
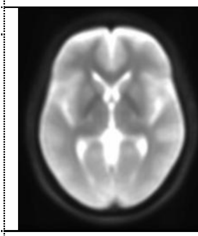
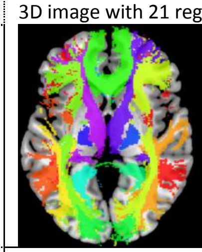
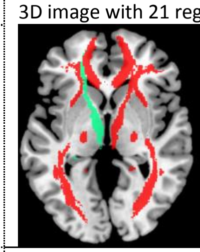
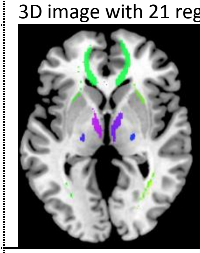
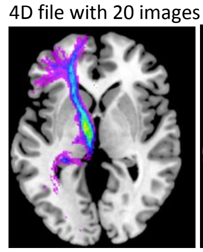
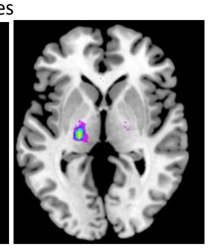
9.3. Files in FRIEND/atlases/HarvardOxford/

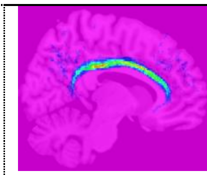
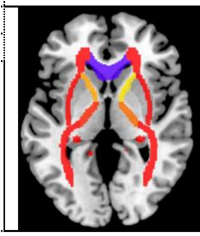
FRIEND/atlases /HarvardOxford	http://neuro.debian.net/pkgs/fsl-harvard-oxford-atlases.html. Probabilistic atlases with 48 cortical and 21 subcortical structural areas.
HarvardOxford-cort-maxprob-thr0-1mm.nii.gz	3D image with 48 cortical regions 
HarvardOxford-cort-maxprob-thr0-1mm.nii_std.nii	
HarvardOxford-cort-maxprob-thr0-2mm.nii.gz	
HarvardOxford-cort-maxprob-thr25-1mm.nii.gz	
HarvardOxford-cort-maxprob-thr25-2mm.nii.gz	
HarvardOxford-cort-maxprob-thr50-1mm.nii.gz	
HarvardOxford-cort-maxprob-thr50-2mm.nii.gz	
HarvardOxford-cort-prob-1mm.nii.gz	
HarvardOxford-cort-prob-2mm.nii.gz	
HarvardOxford-sub-maxprob-thr0-1mm.nii.gz	3D image with 21 subcortical regions 
HarvardOxford-sub-maxprob-thr0-2mm.nii.gz	
HarvardOxford-sub-maxprob-thr25-1mm.nii.gz	
HarvardOxford-sub-maxprob-thr25-2mm.nii.gz	
HarvardOxford-sub-maxprob-thr50-1mm.nii.gz	
HarvardOxford-sub-maxprob-thr50-2mm.nii.gz	
HarvardOxford-sub-prob-1mm.nii.gz	
HarvardOxford-sub-prob-2mm.nii.gz	
labels	Text file with the intensity values of 21 regions: 2, 3, 4, 10, 11, 12, 13, 16, 17, 18, 26, 41, 42, 43, 49, 50, 51, 52, 53, 54, 58

relabel	#!/bin/sh
	
	for ((i=1; i<22; i++)); do
	  v=`sed -ne "${i}p" labels`
	  avwmaths++ $1 -thr $i -uthr $i -bin -mul $v temp-$i
	done
	
	imcp temp-1 $1
	for ((i=2; i<22; i++)); do
	  avwmaths++ $1 -add temp-$i $1
	done

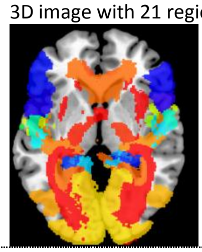
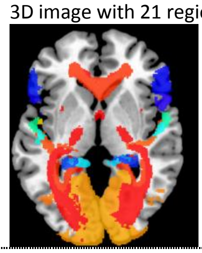
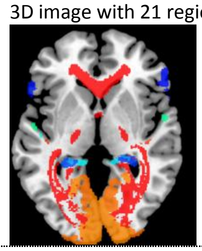
9.4. Files in FRIEND/atlases/JHU/

FRIEND/atlases/JHU	**White matter atlases**
JHU-ICBM-DWI-1mm.nii.gz	
JHU-ICBM-DWI-2mm.nii.gz	

JHU-ICBM-FA-1mm.nii.gz JHU-ICBM-FA-2mm.nii.gz	
JHU-ICBM-T2-1mm.nii.gz JHU-ICBM-T2-2mm.nii.gz	
JHU-ICBM-tracts-maxprob-thr0-1mm.nii.gz JHU-ICBM-tracts-maxprob-thr0-2mm.nii.gz	3D image with 21 regions: 
JHU-ICBM-tracts-maxprob-thr25-1mm.nii.gz JHU-ICBM-tracts-maxprob-thr25-2mm.nii.gz	3D image with 21 regions: 
JHU-ICBM-tracts-maxprob-thr50-1mm.nii.gz JHU-ICBM-tracts-maxprob-thr50-2mm.nii.gz	3D image with 21 regions: 
JHU-ICBM-tracts-prob-1mm.nii.gz JHU-ICBM-tracts-prob-2mm.nii.gz	4D file with 20 images  

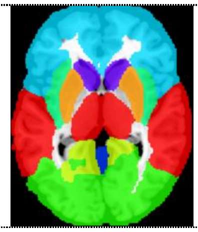
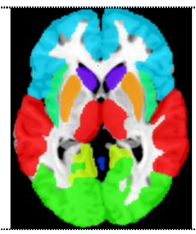
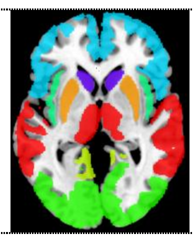
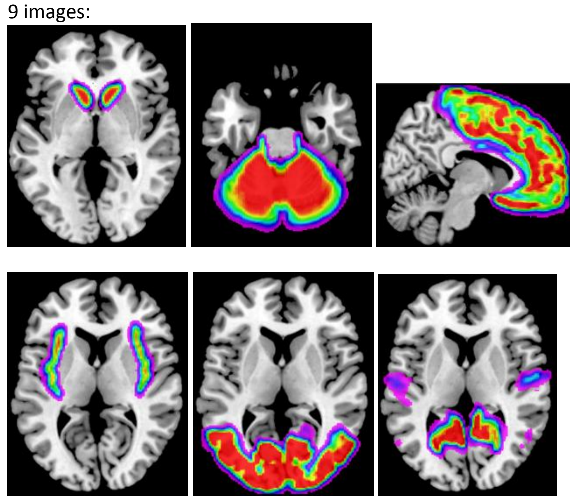
	.....
JHU-ICBM-WhiteMatter-labels-2mm.nii.gz JHU-WhiteMatter-labels-1mm.nii.gz JHU-WhiteMatter-labels-2mm.nii.gz	

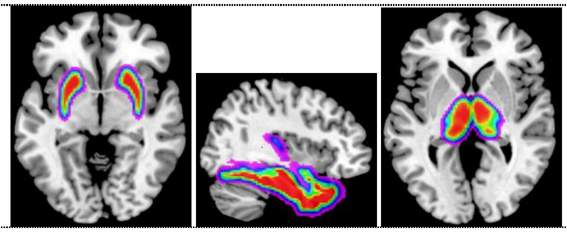
9.5. Files in FRIEND/atlases/Juelich/

FRIEND/atlases/Juelich	Probabilistic atlas with 52 grey matter structures and 10 white matter structures.
Juelich-maxprob-thr0-1mm.nii.gz Juelich-maxprob-thr0-2mm.nii.gz	3D image with 21 regions: 
Juelich-maxprob-thr25-1mm.nii.gz Juelich-maxprob-thr25-2mm.nii.gz	3D image with 21 regions: 
Juelich-maxprob-thr50-1mm.nii.gz Juelich-maxprob-thr50-2mm.nii.gz	3D image with 21 regions: 
Juelich-prob-1mm.nii.gz Juelich-prob-2mm.nii.gz	4D image with 79 images where each image corresponds to a specific area (summarized above).

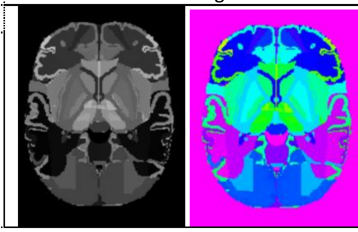
9.6. Files in FRIEND/atlases/MNI/

FRIEND/atlases/MNI/DO	flirt -in MNI-prob-2mm -ref MNI-prob-2mm -out MNI-prob-1mm -applyisoxfm 1

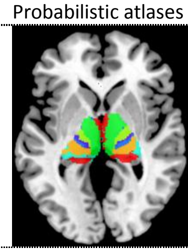
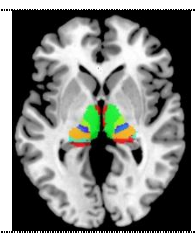
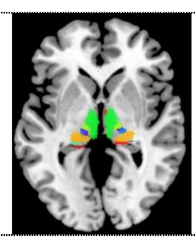
	foreach f (1 2) /usr/local/fsl/data/atlases/bin/threshold MNI-prob-${f}mm /usr/local/fsl/data/atlases/bin/addlut MNI-maxprob-thr0-${f}mm Random-Rainbow /usr/local/fsl/data/atlases/bin/addlut MNI-maxprob-thr25-${f}mm Random-Rainbow /usr/local/fsl/data/atlases/bin/addlut MNI-maxprob-thr50-${f}mm Random-Rainbow end /usr/local/fsl/data/atlases/bin/locate-centres MNI-prob-2mm ../MNI.xml
MNI-maxprob-thr0-1mm.nii.gz MNI-maxprob-thr0-2mm.nii.gz	
MNI-maxprob-thr25-1mm.nii.gz MNI-maxprob-thr25-2mm.nii.gz	
MNI-maxprob-thr50-1mm.nii.gz MNI-maxprob-thr50-2mm.nii.gz	
MNI-prob-1mm.nii.gz MNI-prob-2mm.nii.gz	9 images: 

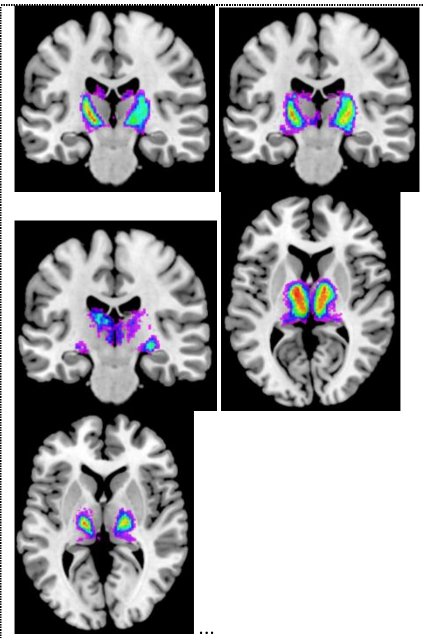
	

9.7. Files in FRIEND/atlases/Talairach/

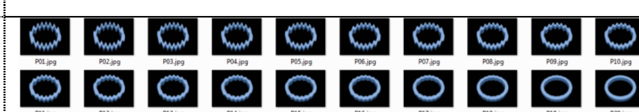
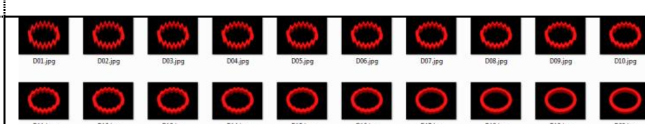
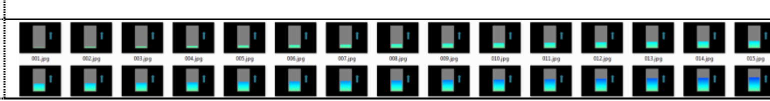
FRIEND/atlases/Talairach	A conversion of the original Talairach structural labellings.
Talairach-labels-1mm.nii.gz	
Talairach-labels-2mm.nii.gz	

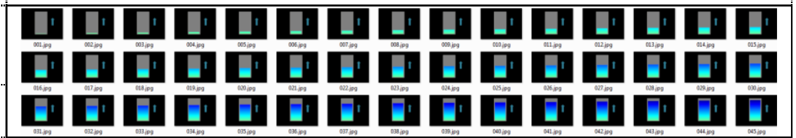
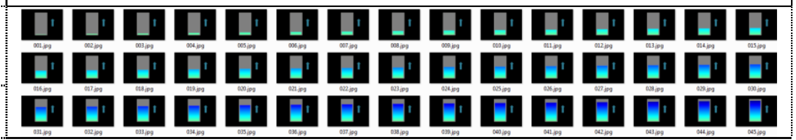
9.8. Files in FRIEND/atlases/Thalamus/

FRIEND/atlases/Thalamus	Probabilistic atlases of 7 sub-thalamic regions.
Thalamus-maxprob-thr0-1mm.nii.gz	
Thalamus-maxprob-thr0-2mm.nii.gz	
Thalamus-maxprob-thr25-1mm.nii.gz	
Thalamus-maxprob-thr25-2mm.nii.gz	
Thalamus-maxprob-thr50-1mm.nii.gz	
Thalamus-maxprob-thr50-2mm.nii.gz	
Thalamus-prob-1mm.nii.gz	3D file with 7 images:
Thalamus-prob-2mm.nii.gz	

	 …

9.9. Files in FRIEND/Feedback/

	Example	Description
FRIEND/FeedBack		Repository of user-provided neurofeedback figures. Directory containing the neurofeedback figures for the conditions (e.g.: NEUTRAL, POSITIVE, NEGATIVE) specified in the [<design>.txt]() file. Directories must be named with the condition names. This means that the number of directories must be equal to the number of conditions (e.g.: 3 directories for 3 conditions). Any number of images on each directory is allowed but all directories must have the same number of images. Neurofeedback figures must be named in alphabetical order, with the first image (e.g. D01.jpg) corresponding to the worst prediction of the cognitive/mental state and the last image (e.g. D10.jpg) corresponding to the best prediction. Most standard format files are recognized by the software (e.g: jpg, tif, png).
<condition1>	**neutral**	
<cond1_feedback_figure1> ..... <cond1_feedback_figurem>	neutral1.jpg neutral20.jpg	
<condition_2>	**pride**	
<cond2_feedback_figure1> ..... <cond2_feedback_figurem>	pride1.jpg pride20.jpg	
<condition_n>	**pity**	
<condn_feedback_figure1> ..... <condn_feedback_figurem>	pity1.jpg pity20.jpg	
<condition1>	**go**	
<cond1_feedback_figure1> ..... <cond1_feedback_figurem>	go1.jpg go20.jpg	

<condition_2>	**guilt**	
<cond2_feedback_figure1> ..... <cond2_feedback_figurem>	guilt1.jpg guilt20.jpg	
<conditionn>	**anger**	
<condn_feedback_figure1> ..... <condn_feedback_figurem>	anger1.jpg anger20.jpg	

9.10. Files in FRIEND/flirtsch/

FRIEND/flirtsch	The FMRIB's Linear Image Registration Tool is a fully automated robust and accurate tool for linear (affine) intra- and inter-modal brain image registration algorithm.
ident.mat	
measurecost1.sch	# 1mm scale setscale 1 setoption smoothing 1 setoption boundguess 1 clear U setrow UA 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 measurecost 7 UA 0 0 0 0 0 0 abs printparams U
pairreg1.sch	# 8mm scale setscale 8 setoption smoothing 8 clear S clear P search # 4mm scale setscale 4 setoption smoothing 4 clear U clear UA clear UB clear US clear UP # remeasure costs at this scale measurecost 7 S 0 0 0 0 0 0 rel copy U US clear U measurecost 7 P 0 0 0 0 0 0 rel copy U UP dualsort US UP # optimise best 3 candidates (pre and post 8mm optimisations) clear U optimise 7 US:1-3 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4 optimise 7 UP:1-3 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4 # also try the identity transform as a starting point at this resolution clear UQ setrow UQ 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 7 UQ 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4 sort U copy U UA # select best 4 optimised solutions and try perturbations of these clear U copy UA:1-4 U optimise 7 UA:1-4 1.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4

	optimise 7 UA:1-4 -1.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4 optimise 7 UA:1-4 0.0 1.0 0.0 0.0 0.0 0.0 0.0 rel 4 optimise 7 UA:1-4 0.0 -1.0 0.0 0.0 0.0 0.0 0.0 rel 4 optimise 7 UA:1-4 0.0 0.0 1.0 0.0 0.0 0.0 0.0 rel 4 optimise 7 UA:1-4 0.0 0.0 -1.0 0.0 0.0 0.0 0.0 rel 4 optimise 7 UA:1-4 0.0 0.0 0.0 0.0 0.0 0.0 0.1 abs 4 optimise 7 UA:1-4 0.0 0.0 0.0 0.0 0.0 0.0 -0.1 abs 4 optimise 7 UA:1-4 0.0 0.0 0.0 0.0 0.0 0.0 0.2 abs 4 optimise 7 UA:1-4 0.0 0.0 0.0 0.0 0.0 0.0 -0.2 abs 4 sort U copy U UB # 2mm scale setscale 2 setoption smoothing 2 clear U clear UC clear UD clear UE clear UF # remeasure costs at this scale measurecost 7 UB 0 0 0 0 0 0 rel sort U copy U UC clear U optimise 7 UC:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4 copy U UD setoption boundguess 1 if MAXDOF > 7 clear U if MAXDOF > 7 optimise 9 UD:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 1 copy U UE if MAXDOF > 9 clear U if MAXDOF > 9 optimise 12 UE:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 2 sort U
pairreg2.sch	# 2mm scale setscale 2 setoption smoothing 2 clear U clear UC clear UD clear UE setrow UC 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 7 UC:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4 copy U UD setoption boundguess 1 if MAXDOF > 7 clear U if MAXDOF > 7 optimise 9 UD:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 1 copy U UE if MAXDOF > 9 clear U if MAXDOF > 9 optimise 12 UE:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 2 sort U
pairreg3.sch	# 2mm scale setscale 2 setoption smoothing 2 setoption paramsubset 6 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 clear U

	clear UC clear UD clear UE clear UF # the line below is the dummy identity - to be useful must have an init setrow UC 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 12 UC:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4 copy U UD setoption boundguess 1 optimise 12 UD:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 2 copy U UE optimise 12 UE:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 1 sort U copy U UF # 1mm scale setscale 1 setoption smoothing 1 setoption boundguess 1 clear U # also try the identity transform as a starting point at this resolution clear UG copy UF:1 UG setrow UG 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 12 UG:1-2 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 1 sort U
sch2D_3dof	# 8mm scale setscale 8 setoption smoothing 8 setoption paramsubset 3 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 clear U clear UA setrow UA 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4 # 4mm scale setscale 4 setoption smoothing 4 setoption paramsubset 3 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 clear UB clear UL clear UM # remeasure costs at this scale clear U measurecost 12 UA 0 0 0 0 0 0 rel sort U copy U UL # optimise best 3 candidates clear U optimise 12 UL:1-3 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4 # also try the identity transform as a starting point at this resolution clear UQ setrow UQ 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 7 UQ 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4 copy U UM # select best 4 optimised solutions and try perturbations of these clear U copy UM:1-4 U optimise 12 UM:1-4 0.0 0.0 1.0 0.0 0.0 0.0 0.0 rel 4 optimise 12 UM:1-4 0.0 0.0 -1.0 0.0 0.0 0.0 0.0 rel 4 sort U clear UB copy U UB # 2mm scale

	setscale 2 setoption smoothing 2 setoption paramsubset 3 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 clear U clear UC clear UD clear UE clear UF # remeasure costs at this scale measurecost 12 UB 0 0 0 0 0 0 rel sort U copy U UC clear U optimise 12 UC:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4 copy U UD setoption boundguess 1 if MAXDOF > 7 clear U if MAXDOF > 7 optimise 9 UD:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 1 copy U UE if MAXDOF > 9 clear U if MAXDOF > 9 optimise 12 UE:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 2 sort U copy U UF # 1mm scale setscale 1 setoption smoothing 1 setoption boundguess 1 setoption paramsubset 3 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 clear U # also try the identity transform as a starting point at this resolution setrow UF 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 12 UF:1-2 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 1 sort U
sch2D_5dof	# 8mm scale setscale 8 setoption smoothing 8 setoption paramsubset 5 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 clear U clear UA setrow UA 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4 # 4mm scale setscale 4 setoption smoothing 4 setoption paramsubset 5 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 clear UB clear UL clear UM # remeasure costs at this scale clear U measurecost 12 UA 0 0 0 0 0 0 rel sort U copy U UL # optimise best 3 candidates clear U optimise 12 UL:1-3 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4

	# also try the identity transform as a starting point at this resolution clear UQ setrow UQ 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 7 UQ 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4 copy U UM # select best 4 optimised solutions and try perturbations of these clear U copy UM:1-4 U optimise 12 UM:1-4 0.0 0.0 1.0 0.0 0.0 0.0 0.0 rel 4 optimise 12 UM:1-4 0.0 0.0 -1.0 0.0 0.0 0.0 0.0 rel 4 optimise 12 UM:1-4 0.0 0.0 0.0 0.1 0.0 0.0 0.0 abs 4 optimise 12 UM:1-4 0.0 0.0 0.0 -0.1 0.0 0.0 0.0 abs 4 optimise 12 UM:1-4 0.0 0.0 0.0 0.0 0.1 0.0 0.0 abs 4 optimise 12 UM:1-4 0.0 0.0 0.0 0.0 -0.1 0.0 0.0 abs 4 sort U clear UB copy U UB # 2mm scale setscale 2 setoption smoothing 2 setoption paramsubset 5 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 clear U clear UC clear UD clear UE clear UF # remeasure costs at this scale measurecost 12 UB 0 0 0 0 0 0 rel sort U copy U UC clear U optimise 12 UC:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4 copy U UD setoption boundguess 1 if MAXDOF > 7 clear U if MAXDOF > 7 optimise 9 UD:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 1 copy U UE if MAXDOF > 9 clear U if MAXDOF > 9 optimise 12 UE:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 2 sort U copy U UF # 1mm scale setscale 1 setoption smoothing 1 setoption boundguess 1 setoption paramsubset 5 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 clear U # also try the identity transform as a starting point at this resolution setrow UF 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 12 UF:1-2 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 1 sort U
sch2D_6dof	# 8mm scale setscale 8 setoption smoothing 8 setoption paramsubset 6 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0

```
clear U
clear UA
setrow UA 1 0 0 0  0 1 0 0  0 0 1 0  0 0 0 1
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   0.0   0.0  rel 4

# 4mm scale
setscale 4
setoption smoothing 4
setoption paramsubset 6  0 0 1 0 0 0 0 0 0 0 0 0  0 0 0 1 0 0 0 0 0 0 0 0  0 0 0 0 1 0 0 0 0 0 0 0  0 0 0 0 0 0 1 0 0 0 0 0  0 0 0 0
0 0 0 1 0 0 0 0  0 0 0 0 0 0 0 0 0 1 0 0
clear UB
clear UL
clear UM
# remeasure costs at this scale
clear U
measurecost 12 UA 0 0 0 0 0 0 rel
sort U
copy U UL
# optimise best 3 candidates
clear U
optimise 12 UL:1-3  0.0   0.0   0.0   0.0   0.0   0.0   0.0  rel 4
# also try the identity transform as a starting point at this resolution
clear UQ
setrow UQ  1 0 0 0  0 1 0 0  0 0 1 0  0 0 0 1
optimise 7 UQ  0.0   0.0   0.0   0.0   0.0   0.0   0.0  rel 4
copy U UM
# select best 4 optimised solutions and try perturbations of these
clear U
copy UM:1-4 U
optimise 12 UM:1-4  0.0   0.0   1.0   0.0   0.0   0.0   0.0  rel 4
optimise 12 UM:1-4  0.0   0.0  -1.0   0.0   0.0   0.0   0.0  rel 4
optimise 12 UM:1-4  0.0   0.0   0.0   0.1   0.0   0.0   0.0  abs 4
optimise 12 UM:1-4  0.0   0.0   0.0  -0.1   0.0   0.0   0.0  abs 4
optimise 12 UM:1-4  0.0   0.0   0.0   0.0   0.1   0.0   0.0  abs 4
optimise 12 UM:1-4  0.0   0.0   0.0   0.0  -0.1   0.0   0.0  abs 4
sort U
clear UB
copy U UB

# 2mm scale
setscale 2
setoption smoothing 2
setoption paramsubset 6  0 0 1 0 0 0 0 0 0 0 0 0  0 0 0 1 0 0 0 0 0 0 0 0  0 0 0 0 1 0 0 0 0 0 0 0  0 0 0 0 0 0 1 0 0 0 0 0  0 0 0 0
0 0 0 1 0 0 0 0  0 0 0 0 0 0 0 0 0 1 0 0
clear U
clear UC
clear UD
clear UE
clear UF
# remeasure costs at this scale
measurecost 12 UB 0 0 0 0 0 0 rel
sort U
copy U UC
clear U
optimise 12  UC:1  0.0   0.0   0.0   0.0   0.0   0.0   0.0  rel 4
copy U UD
setoption boundguess 1
if MAXDOF > 7
 clear U
if MAXDOF > 7
 optimise 9  UD:1  0.0   0.0   0.0   0.0   0.0   0.0   0.0  rel 1
copy U UE
if MAXDOF > 9
 clear U
```

	if MAXDOF > 9 optimise 12 UE:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 2 sort U copy U UF # 1mm scale setscale 1 setoption smoothing 1 setoption boundguess 1 setoption paramsubset 6 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 clear U # also try the identity transform as a starting point at this resolution setrow UF 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 12 UF:1-2 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 1 sort U
sch3Dtrans_3dof	clear UT ## X TRANSLATION ## # 8mm scale setscale 8 setoption smoothing 8 setoption boundguess 8 setoption paramsubset 1 0 0 0 1 0 0 0 0 0 0 0 0 clear U clear UA setrow UA 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 8.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -8.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 16.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -16.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 24.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -24.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 32.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -32.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 40.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -40.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 48.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -48.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 56.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -56.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 64.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -64.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 72.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -72.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 80.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -80.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 88.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -88.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 96.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -96.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 104.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -104.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 112.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -112.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 120.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -120.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 128.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -128.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 136.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -136.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 144.0 0.0 0.0 0.0 abs 4

```
optimise 12 UA:1   0.0   0.0   0.0 -144.0   0.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0  152.0   0.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0 -152.0   0.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0  160.0   0.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0 -160.0   0.0   0.0   0.0   abs 4
clear UA
copy U UA

# 4mm scale
setscale 4
setoption smoothing 4
setoption boundguess 4
setoption paramsubset 1  0 0 0 1 0 0 0 0 0 0 0 0
clear UB
clear UL
clear UM
# remeasure costs at this scale
clear U
measurecost 12 UA 0 0 0 0 0 0 abs
sort U
copy U UL
# optimise best 3 candidates
clear U
optimise 12 UL:1-3  0.0   0.0   0.0   0.0   0.0   0.0   0.0  abs 4
# also try the identity transform as a starting point at this resolution
clear UQ
setrow UQ  1 0 0 0  0 1 0 0  0 0 1 0  0 0 0 1
optimise 12 UQ  0.0   0.0   0.0   0.0   0.0   0.0   0.0  rel 4
clear UB
copy U UB

# 2mm scale
setscale 2
setoption smoothing 2
setoption boundguess 2
setoption paramsubset 1  0 0 0 1 0 0 0 0 0 0 0 0
clear U
clear UC
clear UF
# remeasure costs at this scale
measurecost 12 UB 0 0 0 0 0 0 abs
sort U
copy U UC
clear U
optimise 12  UC:1  0.0   0.0   0.0   0.0   0.0   0.0   0.0  abs 4
copy U UF

# 1mm scale
setscale 1
setoption smoothing 1
setoption boundguess 1
setoption paramsubset 1  0 0 0 1 0 0 0 0 0 0 0 0
clear U
# also try the identity transform as a starting point at this resolution
setrow UF  1 0 0 0  0 1 0 0  0 0 1 0  0 0 0 1
optimise 12 UF:1-2  0.0   0.0   0.0   0.0   0.0   0.0   0.0  abs 1
sort U
copy U:1 UT


## Y TRANSLATION ##

# 8mm scale
setscale 8
```

```
setoption smoothing 8
setoption boundguess 8
setoption paramsubset 1  0 0 0 0 1 0 0 0 0 0 0 0
clear U
clear UA
setrow UA 1 0 0 0  0 1 0 0  0 0 1 0  0 0 0 1
optimise 12 UA:1   0.0   0.0   0.0   0.0    0.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0    8.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   -8.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   16.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -16.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   24.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -24.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   32.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -32.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   40.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -40.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   48.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -48.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   56.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -56.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   64.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -64.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   72.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -72.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   80.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -80.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   88.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -88.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   96.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -96.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  104.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0 -104.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  112.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0 -112.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  120.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0 -120.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  128.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0 -128.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  136.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0 -136.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  144.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0 -144.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  152.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0 -152.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  160.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0 -160.0   0.0   0.0   abs 4
clear UA
copy U UA

# 4mm scale
setscale 4
setoption smoothing 4
setoption boundguess 4
setoption paramsubset 1  0 0 0 0 1 0 0 0 0 0 0 0
clear UB
clear UL
clear UM
# remeasure costs at this scale
clear U
measurecost 12 UA 0 0 0 0 0 0 abs
sort U
copy U UL
# optimise best 3 candidates
```

	clear U optimise 12 UL:1-3 0.0 0.0 0.0 0.0 0.0 0.0 0.0 abs 4 # also try the identity transform as a starting point at this resolution clear UQ setrow UQ 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 7 UQ 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4 clear UB copy U UB # 2mm scale setscale 2 setoption smoothing 2 setoption boundguess 2 setoption paramsubset 1 0 0 0 0 1 0 0 0 0 0 0 0 clear U clear UC clear UF # remeasure costs at this scale measurecost 12 UB 0 0 0 0 0 0 abs sort U copy U UC clear U optimise 12 UC:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 abs 4 copy U UF # 1mm scale setscale 1 setoption smoothing 1 setoption boundguess 1 setoption paramsubset 1 0 0 0 0 1 0 0 0 0 0 0 0 clear U # also try the identity transform as a starting point at this resolution setrow UF 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 12 UF:1-2 0.0 0.0 0.0 0.0 0.0 0.0 0.0 abs 1 sort U copy U:1 UT ## Z TRANSLATION ## # 8mm scale setscale 8 setoption smoothing 8 setoption boundguess 8 setoption paramsubset 1 0 0 0 0 0 1 0 0 0 0 0 0 clear U clear UA setrow UA 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 8.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 -8.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 16.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 -16.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 24.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 -24.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 32.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 -32.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 40.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 -40.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 48.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 -48.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 56.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 -56.0 0.0 abs 4

```
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   64.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -64.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   72.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -72.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   80.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -80.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   88.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -88.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   96.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -96.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  104.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -104.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  112.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -112.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  120.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -120.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  128.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -128.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  136.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -136.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  144.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -144.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  152.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -152.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  160.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -160.0   0.0   abs 4
clear UA
copy U UA

# 4mm scale
setscale 4
setoption smoothing 4
setoption boundguess 4
setoption paramsubset 1  0 0 0 0 0 1 0 0 0 0 0 0
clear UB
clear UL
clear UM
# remeasure costs at this scale
clear U
measurecost 12 UA 0 0 0 0 0 0 abs
sort U
copy U UL
# optimise best 3 candidates
clear U
optimise 12 UL:1-3  0.0   0.0   0.0   0.0   0.0   0.0   0.0  abs 4
# also try the identity transform as a starting point at this resolution
clear UQ
setrow UQ  1 0 0 0  0 1 0 0  0 0 1 0  0 0 0 1
optimise 7 UQ  0.0   0.0   0.0   0.0   0.0   0.0   0.0  rel 4
clear UB
copy U UB

# 2mm scale
setscale 2
setoption smoothing 2
setoption boundguess 2
setoption paramsubset 1  0 0 0 0 0 1 0 0 0 0 0 0
clear U
clear UC
clear UF
# remeasure costs at this scale
measurecost 12 UB 0 0 0 0 0 0 abs
sort U
copy U UC
```

```
clear U
optimise 12  UC:1  0.0   0.0   0.0   0.0   0.0   0.0   0.0  abs 4
copy U UF

# 1mm scale
setscale 1
setoption smoothing 1
setoption boundguess 1
setoption paramsubset 1  0 0 0 0 0 1 0 0 0 0 0 0
clear U
# also try the identity transform as a starting point at this resolution
setrow UF  1 0 0 0  0 1 0 0  0 0 1 0  0 0 0 1
optimise 12 UF:1-2  0.0   0.0   0.0   0.0   0.0   0.0   0.0  abs 1
sort U
copy U:1 UT

## sort the 3 results to pick the best
clear U
copy UT U
sort U

# now do a general 3 DOF translation to refine this
clear UA
copy U UA

# 8mm scale
setscale 8
setoption smoothing 8
setoption paramsubset 3  0 0 0 1 0 0 0 0 0 0 0 0  0 0 0 0 1 0 0 0 0 0 0 0  0 0 0 0 0 1 0 0 0 0 0 0
clear U
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   0.0   0.0  rel 4

# 4mm scale
setscale 4
setoption smoothing 4
setoption paramsubset 3  0 0 0 1 0 0 0 0 0 0 0 0  0 0 0 0 1 0 0 0 0 0 0 0  0 0 0 0 0 1 0 0 0 0 0 0
clear UB
clear UL
clear UM
# remeasure costs at this scale
clear U
measurecost 12 UA 0 0 0 0 0 0 rel
sort U
copy U UL
# optimise best 3 candidates
clear U
optimise 12 UL:1-3  0.0   0.0   0.0   0.0   0.0   0.0   0.0  rel 4
# also try the identity transform as a starting point at this resolution
clear UQ
setrow UQ  1 0 0 0  0 1 0 0  0 0 1 0  0 0 0 1
optimise 7 UQ  0.0   0.0   0.0   0.0   0.0   0.0   0.0  rel 4
copy U UB

# 2mm scale
setscale 2
setoption smoothing 2
setoption paramsubset 3  0 0 0 1 0 0 0 0 0 0 0 0  0 0 0 0 1 0 0 0 0 0 0 0  0 0 0 0 0 1 0 0 0 0 0 0
clear U
clear UC
clear UD
clear UE
clear UF
# remeasure costs at this scale
measurecost 12 UB 0 0 0 0 0 0 rel
```

	sort U copy U UC clear U optimise 12 UC:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4 sort U copy U UF # 1mm scale setscale 1 setoption smoothing 1 setoption boundguess 1 setoption paramsubset 3 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 clear U # also try the identity transform as a starting point at this resolution setrow UF 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 12 UF:1-2 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 1 sort U
simple3D.sch	# 8mm scale setscale 8 setoption smoothing 8 clear UU clear U setrow UU 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 7 UU:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4 copy U UA # 4mm scale setscale 4 setoption smoothing 4 clear U clear UB # optimise best 1 candidate (pre and post 8mm optimisations) clear U optimise 7 UA:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4 sort U copy U UB # 2mm scale setscale 2 setoption smoothing 2 clear U clear UC clear UD clear UE clear UF # remeasure costs at this scale measurecost 7 UB 0 0 0 0 0 0 rel sort U copy U UC clear U optimise 7 UC:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4 copy U UD setoption boundguess 1 if MAXDOF > 7 clear U if MAXDOF > 7 optimise 9 UD:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 1 copy U UE if MAXDOF > 9 clear U if MAXDOF > 9 optimise 12 UE:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 2 sort U copy U UF # 1mm scale setscale 1

	setoption smoothing 1 setoption boundguess 1 clear U # also try the identity transform as a starting point at this resolution setrow UF 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 12 UF:1-2 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 1 sort U
xyztrans.sch	clear UT ## X TRANSLATION ## # 8mm scale setscale 8 setoption smoothing 8 setoption boundguess 8 setoption paramsubset 1 0 0 0 1 0 0 0 0 0 0 0 0 clear U clear UA setrow UA 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 8.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -8.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 16.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -16.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 24.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -24.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 32.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -32.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 40.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -40.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 48.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -48.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 56.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -56.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 64.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -64.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 72.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -72.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 80.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -80.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 88.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -88.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 96.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -96.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 104.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -104.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 112.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -112.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 120.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -120.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 128.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -128.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 136.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -136.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 144.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -144.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 152.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -152.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 160.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 -160.0 0.0 0.0 0.0 abs 4 clear UA copy U UA # 4mm scale

```
setscale 4
setoption smoothing 4
setoption boundguess 4
setoption paramsubset 1  0 0 0 1 0 0 0 0 0 0 0 0
clear UB
clear UL
clear UM
# remeasure costs at this scale
clear U
measurecost 12 UA 0 0 0 0 0 0 abs
sort U
copy U UL
# optimise best 3 candidates
clear U
optimise 12 UL:1-3  0.0   0.0   0.0   0.0   0.0   0.0   0.0  abs 4
# also try the identity transform as a starting point at this resolution
clear UQ
setrow UQ  1 0 0 0  0 1 0 0  0 0 1 0  0 0 0 1
optimise 12 UQ  0.0   0.0   0.0   0.0   0.0   0.0   0.0  rel 4
clear UB
copy U UB

# 2mm scale
setscale 2
setoption smoothing 2
setoption boundguess 2
setoption paramsubset 1  0 0 0 1 0 0 0 0 0 0 0 0
clear U
clear UC
clear UF
# remeasure costs at this scale
measurecost 12 UB 0 0 0 0 0 0 abs
sort U
copy U UC
clear U
optimise 12  UC:1  0.0   0.0   0.0   0.0   0.0   0.0   0.0  abs 4
copy U UF

# 1mm scale
setscale 1
setoption smoothing 1
setoption boundguess 1
setoption paramsubset 1  0 0 0 1 0 0 0 0 0 0 0 0
clear U
# also try the identity transform as a starting point at this resolution
setrow UF  1 0 0 0  0 1 0 0  0 0 1 0  0 0 0 1
optimise 12 UF:1-2  0.0   0.0   0.0   0.0   0.0   0.0   0.0  abs 1
sort U
copy U:1 UT


## Y TRANSLATION ##

# 8mm scale
setscale 8
setoption smoothing 8
setoption boundguess 8
setoption paramsubset 1  0 0 0 0 1 0 0 0 0 0 0 0
clear U
clear UA
setrow UA 1 0 0 0  0 1 0 0  0 0 1 0  0 0 0 1
optimise 12 UA:1   0.0   0.0   0.0   0.0    0.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0    8.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   -8.0   0.0   0.0   abs 4
```

```
optimise 12 UA:1   0.0   0.0   0.0   0.0   16.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -16.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   24.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -24.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   32.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -32.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   40.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -40.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   48.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -48.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   56.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -56.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   64.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -64.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   72.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -72.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   80.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -80.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   88.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -88.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0   96.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  -96.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  104.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0 -104.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  112.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0 -112.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  120.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0 -120.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  128.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0 -128.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  136.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0 -136.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  144.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0 -144.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  152.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0 -152.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0  160.0   0.0   0.0   abs 4
optimise 12 UA:1   0.0   0.0   0.0   0.0 -160.0   0.0   0.0   abs 4
clear UA
copy U UA

# 4mm scale
setscale 4
setoption smoothing 4
setoption boundguess 4
setoption paramsubset 1  0 0 0 0 1 0 0 0 0 0 0 0
clear UB
clear UL
clear UM
# remeasure costs at this scale
clear U
measurecost 12 UA 0 0 0 0 0 0 abs
sort U
copy U UL
# optimise best 3 candidates
clear U
optimise 12 UL:1-3  0.0   0.0   0.0   0.0   0.0   0.0   0.0  abs 4
# also try the identity transform as a starting point at this resolution
clear UQ
setrow UQ  1 0 0 0  0 1 0 0  0 0 1 0  0 0 0 1
optimise 7 UQ  0.0   0.0   0.0   0.0   0.0   0.0   0.0  rel 4
clear UB
copy U UB
```

```
# 2mm scale
setscale 2
setoption smoothing 2
setoption boundguess 2
setoption paramsubset 1  0 0 0 0 1 0 0 0 0 0 0 0
clear U
clear UC
clear UF
# remeasure costs at this scale
measurecost 12 UB 0 0 0 0 0 0 abs
sort U
copy U UC
clear U
optimise 12  UC:1  0.0   0.0   0.0   0.0   0.0   0.0   0.0  abs 4
copy U UF

# 1mm scale
setscale 1
setoption smoothing 1
setoption boundguess 1
setoption paramsubset 1  0 0 0 0 1 0 0 0 0 0 0 0
clear U
# also try the identity transform as a starting point at this resolution
setrow UF  1 0 0 0  0 1 0 0  0 0 1 0  0 0 0 1
optimise 12 UF:1-2  0.0   0.0   0.0   0.0   0.0   0.0   0.0  abs 1
sort U
copy U:1 UT



## Z TRANSLATION ##

# 8mm scale
setscale 8
setoption smoothing 8
setoption boundguess 8
setoption paramsubset 1  0 0 0 0 0 1 0 0 0 0 0 0
clear U
clear UA
setrow UA 1 0 0 0  0 1 0 0  0 0 1 0  0 0 0 1
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0    0.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0    8.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   -8.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   16.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -16.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   24.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -24.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   32.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -32.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   40.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -40.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   48.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -48.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   56.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -56.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   64.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -64.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   72.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -72.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   80.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -80.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   88.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -88.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   96.0   0.0   abs 4
```

```
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -96.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  104.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -104.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  112.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -112.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  120.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -120.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  128.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -128.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  136.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -136.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  144.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -144.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  152.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -152.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  160.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -160.0   0.0   abs 4
clear UA
copy U UA

# 4mm scale
setscale 4
setoption smoothing 4
setoption boundguess 4
setoption paramsubset 1  0 0 0 0 0 1 0 0 0 0 0 0
clear UB
clear UL
clear UM
# remeasure costs at this scale
clear U
measurecost 12 UA 0 0 0 0 0 0 abs
sort U
copy U UL
# optimise best 3 candidates
clear U
optimise 12 UL:1-3  0.0   0.0   0.0   0.0   0.0   0.0   0.0  abs 4
# also try the identity transform as a starting point at this resolution
clear UQ
setrow UQ  1 0 0 0  0 1 0 0  0 0 1 0  0 0 0 1
optimise 7 UQ  0.0   0.0   0.0   0.0   0.0   0.0   0.0  rel 4
clear UB
copy U UB

# 2mm scale
setscale 2
setoption smoothing 2
setoption boundguess 2
setoption paramsubset 1  0 0 0 0 0 1 0 0 0 0 0 0
clear U
clear UC
clear UF
# remeasure costs at this scale
measurecost 12 UB 0 0 0 0 0 0 abs
sort U
copy U UC
clear U
optimise 12  UC:1  0.0   0.0   0.0   0.0   0.0   0.0   0.0  abs 4
copy U UF

# 1mm scale
setscale 1
setoption smoothing 1
setoption boundguess 1
setoption paramsubset 1  0 0 0 0 0 1 0 0 0 0 0 0
```

```
clear U
# also try the identity transform as a starting point at this resolution
setrow UF  1 0 0 0  0 1 0 0  0 0 1 0  0 0 0 1
optimise 12 UF:1-2  0.0   0.0   0.0   0.0   0.0   0.0   0.0  abs 1
sort U
copy U:1 UT

## sort the 3 results to pick the best
clear U
copy UT U
sort U

# now do a general 3 DOF translation to refine this
clear UA
copy U UA

# 8mm scale
setscale 8
setoption smoothing 8
setoption paramsubset 3  0 0 0 1 0 0 0 0 0 0 0 0  0 0 0 0 1 0 0 0 0 0 0 0  0 0 0 0 0 1 0 0 0 0 0 0
clear U
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   0.0   0.0  rel 4

# 4mm scale
setscale 4
setoption smoothing 4
setoption paramsubset 3  0 0 0 1 0 0 0 0 0 0 0 0  0 0 0 0 1 0 0 0 0 0 0 0  0 0 0 0 0 1 0 0 0 0 0 0
clear UB
clear UL
clear UM
# remeasure costs at this scale
clear U
measurecost 12 UA 0 0 0 0 0 0 rel
sort U
copy U UL
# optimise best 3 candidates
clear U
optimise 12 UL:1-3  0.0   0.0   0.0   0.0   0.0   0.0   0.0  rel 4
# also try the identity transform as a starting point at this resolution
clear UQ
setrow UQ  1 0 0 0  0 1 0 0  0 0 1 0  0 0 0 1
optimise 7 UQ  0.0   0.0   0.0   0.0   0.0   0.0   0.0  rel 4
copy U UB

# 2mm scale
setscale 2
setoption smoothing 2
setoption paramsubset 3  0 0 0 1 0 0 0 0 0 0 0 0  0 0 0 0 1 0 0 0 0 0 0 0  0 0 0 0 0 1 0 0 0 0 0 0
clear U
clear UC
clear UD
clear UE
clear UF
# remeasure costs at this scale
measurecost 12 UB 0 0 0 0 0 0 rel
sort U
copy U UC
clear U
optimise 12  UC:1  0.0   0.0   0.0   0.0   0.0   0.0   0.0  rel 4
sort U
copy U UF

# 1mm scale
setscale 1
```

	setoption smoothing 1 setoption boundguess 1 setoption paramsubset 3 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 clear U # also try the identity transform as a starting point at this resolution setrow UF 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 12 UF:1-2 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 1 sort U
ytransonly.sch	## Y TRANSLATION ## # 8mm scale setscale 8 setoption smoothing 8 setoption boundguess 8 setoption paramsubset 1 0 0 0 0 1 0 0 0 0 0 0 0 clear U clear UA setrow UA 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 8.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 -8.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 16.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 -16.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 24.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 -24.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 32.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 -32.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 40.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 -40.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 48.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 -48.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 56.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 -56.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 64.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 -64.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 72.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 -72.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 80.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 -80.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 88.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 -88.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 96.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 -96.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 104.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 -104.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 112.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 -112.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 120.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 -120.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 128.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 -128.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 136.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 -136.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 144.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 -144.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 152.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 -152.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 160.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 -160.0 0.0 0.0 abs 4 clear UA copy U UA # 4mm scale setscale 4

	setoption smoothing 4 setoption boundguess 4 setoption paramsubset 1 0 0 0 0 1 0 0 0 0 0 0 0 clear UB clear UL clear UM # remeasure costs at this scale clear U measurecost 12 UA 0 0 0 0 0 0 abs sort U copy U UL # optimise best 3 candidates clear U optimise 12 UL:1-3 0.0 0.0 0.0 0.0 0.0 0.0 0.0 abs 4 # also try the identity transform as a starting point at this resolution clear UQ setrow UQ 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 7 UQ 0.0 0.0 0.0 0.0 0.0 0.0 0.0 rel 4 clear UB copy U UB # 2mm scale setscale 2 setoption smoothing 2 setoption boundguess 2 setoption paramsubset 1 0 0 0 0 1 0 0 0 0 0 0 0 clear U clear UC clear UF # remeasure costs at this scale measurecost 12 UB 0 0 0 0 0 0 abs sort U copy U UC clear U optimise 12 UC:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 abs 4 copy U UF # 1mm scale setscale 1 setoption smoothing 1 setoption boundguess 1 setoption paramsubset 1 0 0 0 0 1 0 0 0 0 0 0 0 clear U # also try the identity transform as a starting point at this resolution setrow UF 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 12 UF:1-2 0.0 0.0 0.0 0.0 0.0 0.0 0.0 abs 1 sort U
ztransonly.sch	# 8mm scale setscale 8 setoption smoothing 8 setoption boundguess 8 setoption paramsubset 1 0 0 0 0 0 1 0 0 0 0 0 0 clear U clear UA setrow UA 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 8.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 -8.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 16.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 -16.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 24.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 -24.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 32.0 0.0 abs 4 optimise 12 UA:1 0.0 0.0 0.0 0.0 0.0 -32.0 0.0 abs 4

```
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   40.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -40.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   48.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -48.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   56.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -56.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   64.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -64.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   72.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -72.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   80.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -80.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   88.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -88.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0   96.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  -96.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  104.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -104.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  112.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -112.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  120.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -120.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  128.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -128.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  136.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -136.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  144.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -144.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  152.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -152.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0  160.0   0.0   abs 4
optimise 12 UA:1  0.0   0.0   0.0   0.0   0.0 -160.0   0.0   abs 4
clear UA
copy U UA

# 4mm scale
setscale 4
setoption smoothing 4
setoption boundguess 4
setoption paramsubset 1  0 0 0 0 0 1 0 0 0 0 0 0
clear UB
clear UL
clear UM
# remeasure costs at this scale
clear U
measurecost 12 UA 0 0 0 0 0 0 abs
sort U
copy U UL
# optimise best 3 candidates
clear U
optimise 12 UL:1-3  0.0   0.0   0.0   0.0   0.0   0.0   0.0  abs 4
# also try the identity transform as a starting point at this resolution
clear UQ
setrow UQ  1 0 0 0  0 1 0 0  0 0 1 0  0 0 0 1
optimise 7 UQ  0.0   0.0   0.0   0.0   0.0   0.0   0.0  rel 4
clear UB
copy U UB

# 2mm scale
setscale 2
setoption smoothing 2
setoption boundguess 2
setoption paramsubset 1  0 0 0 0 0 1 0 0 0 0 0 0
clear U
```

	clear UC clear UF # remeasure costs at this scale measurecost 12 UB 0 0 0 0 0 0 abs sort U copy U UC clear U optimise 12 UC:1 0.0 0.0 0.0 0.0 0.0 0.0 0.0 abs 4 copy U UF # 1mm scale setscale 1 setoption smoothing 1 setoption boundguess 1 setoption paramsubset 1 0 0 0 0 0 1 0 0 0 0 0 0 clear U # also try the identity transform as a starting point at this resolution setrow UF 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 optimise 12 UF:1-2 0.0 0.0 0.0 0.0 0.0 0.0 0.0 abs 1 sort U

9.11. Files in FRIEND/fnirtcnf/

FRIEND/fnirtcnf	The FSL nonlinear registration methodology
FA_2_FMRIB58_1mm.cnf	# name of reference image # --ref=/usr/local/fsl/data/standard/FMRIB58_FA_1mm.nii.gz --ref=FMRIB58_FA_1mm # If =1, use implicit masking based on value in --ref image. Default =1 --imprefm=1 # If =1, use implicit masking based on value in --in image, Default =1 --impinm=1 # Value to mask out in --ref image. Default =0.0 --imprefval=0 # Value to mask out in --in image. Default =0.0 --impinval=0 # sub-sampling scheme, default 4,2,1,1 --subsamp=8,4,2,2 # Max # of non-linear iterations, default 5,5,5,5 --miter=5,5,5,5 # FWHM (in mm) of gaussian smoothing kernel for input volume, default 6,4,2,2 --infwhm=12,6,2,2 # FWHM (in mm) of gaussian smoothing kernel for ref volume, default 4,2,0,0 --reffwhm=12,6,2,2 # Weigth of membrane energy regularisation, default depending on --ssqlambda and --regmod switches. See user documetation. --lambda=300,75,30,30 # Estimate intensity-mapping if set, deafult 1 (true) --estint=1,1,1,0 # (approximate) resolution (in mm) of warp basis in x-, y- and z-direction, default 10,10,10 --warpres=10,10,10 # If set (=1), lambda is weighted by current ssq, default 1 --ssqlambda=1 # Model for regularisation of warp-field [membrane_energy bending_energy], default bending_energy --regmod=bending_energy # Model for intensity-mapping [none global_linear global_non_linear local_linear global_non_linear_with_bias local_non_linear] --intmod=global_linear # If =1, ref image is used to calculate derivatives. Default =0 --refderiv=0
GM_2_MNI152GM_2mm.cnf	# name of file with mask in reference space # --refmask=/usr/local/fsl/data/standard/MNI152_T1_2mm_brain_mask_dil.nii.gz --refmask=MNI152_T1_2mm_brain_mask_dil

	# If =1, use implicit masking based on value in --ref image. Default =1 # Here we consider 0 to carry information (we trust the segmentation) --imprefm=0 # If =1, use implicit masking based on value in --in image, Default =1 # Here we consider 0 to carry information (we trust the segmentation) --impinm=0 # Value to mask out in --ref image. Default =0.0 --imprefval=0 # Value to mask out in --in image. Default =0.0 --impinval=0 # sub-sampling scheme, default 4,2,1,1 --subsamp=4,2,1,1 # Max # of non-linear iterations, default 5,5,5,5 --miter=5,5,10,5 # FWHM (in mm) of gaussian smoothing kernel for input volume, default 6,4,2,2 --infwhm=6,4,2,2 # FWHM (in mm) of gaussian smoothing kernel for ref volume, default 4,2,0,0 --reffwhm=4,2,0,0 # Weigth of membrane energy regularisation, default depending on --ssqlambda and --regmod switches. See user documetation. --lambda=150,75,50,30 # Estimate intensity-mapping if set, deafult 1 (true) --estint=1,1,1,0 # Apply the mask if set, default 1 (true) --applyrefmask=0,0,0,1 # Apply the mask if set, default 1 (true) --applyinmask=1 # (approximate) resolution (in mm) of warp basis in x-, y- and z-direction, default 10,10,10 --warpres=10,10,10 # If set (=1), lambda is weighted by current ssq, default 1 --ssqlambda=1 # Model for regularisation of warp-field [membrane_energy bending_energy], default bending_energy --regmod=bending_energy # Model for intensity-mapping [none global_linear global_non_linear local_linear global_non_linear_with_bias local_non_linear] --intmod=global_linear # Order of poynomial for mapping intensities, default 5 --intorder=5 # Resolution (in mm) of bias-field modelling local intensities, default 50,50,50 --biasres=50,50,50 # Weight of regularisation for bias-field, default 10000 --biaslambda=10000 # If =1, ref image is used to calculate derivatives. Default =0 --refderiv=0 # Project onto space of stransforms with Jacobian determinants in the range 0.2--5. --jacrange=0.2,5
T1_2_MNI152_2mm.cnf	# name of reference image # --ref=/usr/local/fsl/data/standard/MNI152_T1_2mm.nii.gz #--ref=MNI152_T1_2mm # name of file with mask in reference space # --refmask=/usr/local/fsl/data/standard/MNI152_T1_2mm_brain_mask_dil.nii.gz #--refmask=MNI152_T1_2mm_brain_mask_dil # If =1, use implicit masking based on value in --ref image. Default =1 --imprefm=1 # If =1, use implicit masking based on value in --in image, Default =1 --impinm=1 # Value to mask out in --ref image. Default =0.0 --imprefval=0 # Value to mask out in --in image. Default =0.0 --impinval=0 # sub-sampling scheme, default 4,2,1,1 --subsamp=4,4,2,2,1,1 # Max # of non-linear iterations, default 5,5,5,5

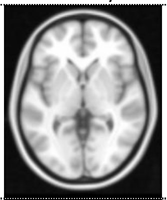
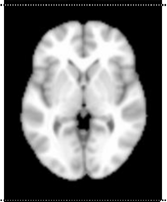
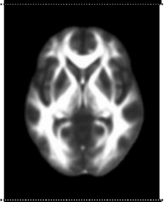
	--miter=5,5,5,5,5,10 # FWHM (in mm) of gaussian smoothing kernel for input volume, default 6,4,2,2 --infwhm=8,6,5,4.5,3,2 # FWHM (in mm) of gaussian smoothing kernel for ref volume, default 4,2,0,0 --reffwhm=8,6,5,4,2,0 # Weigth of membrane energy regularisation, default depending on --ssqlambda and --regmod switches. See user documetation. --lambda=300,150,100,50,40,30 # Estimate intensity-mapping if set, deafult 1 (true) --estint=1,1,1,1,1,0 # Apply the mask if set, default 1 (true) --applyrefmask=1,1,1,1,1,1 # Apply the mask if set, default 1 (true) --applyinmask=1 # (approximate) resolution (in mm) of warp basis in x-, y- and z-direction, default 10,10,10 --warpres=10,10,10 # If set (=1), lambda is weighted by current ssq, default 1 --ssqlambda=1 # Model for regularisation of warp-field [membrane_energy bending_energy], default bending_energy --regmod=bending_energy # Model for intensity-mapping [none global_linear global_non_linear local_linear global_non_linear_with_bias local_non_linear] --intmod=global_non_linear_with_bias # Order of poynomial for mapping intensities, default 5 --intorder=5 # Resolution (in mm) of bias-field modelling local intensities, default 50,50,50 --biasres=50,50,50 # Weight of regularisation for bias-field, default 10000 --biaslambda=10000 # If =1, ref image is used to calculate derivatives. Default =0 --refderiv=0

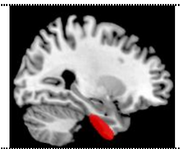
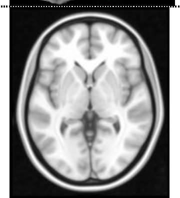
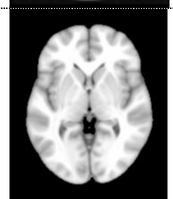
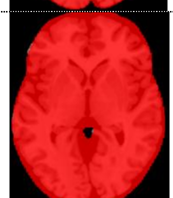
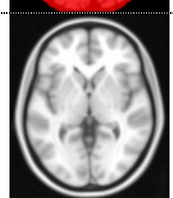
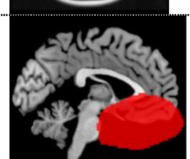
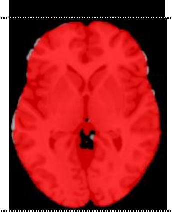
9.12. Files in FRIEND/luts/

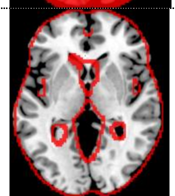
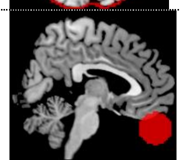
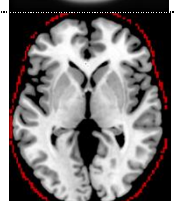
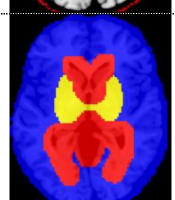
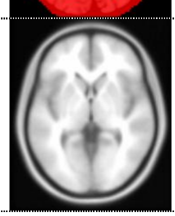
FRIEND/luts	RGB colormap look up tables.
1hot.lut	
2winter.lut	
3warm.lut	
4cool.lut	
5redyell.lut	
6bluegrn.lut	
aal.lut	
actc.lut	
BLACKBDY.LUT	
bluegray.lut	
bone.lut	
brodmann.lut	
CARDIAC.LUT	
cortex.lut	
FLOW.LUT	
French.lut	
GE_color.lut	
Gold.lut	
gooch.lut	
greengray.lut	
HOTIRON.lut	
lu.lut	
NIH.lut	NIH lookup table.
NIH_fire.lut	
NIH_ice.lut	

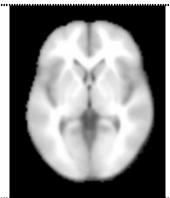
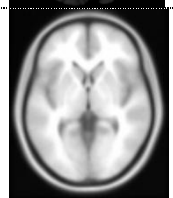
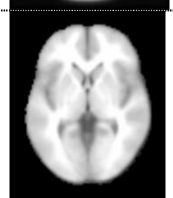
pink.lut	
Rainramp.lut	
ramp.gif	
ramp2.gif	
redgray.lut	
render1.lut	
render1.map	
render1t.lut	
render1t.map	
render2.lut	
render2.map	
render2t.lut	
render2t.map	
render3.lut	
render3.map	
render3t.lut	
render3t.map	
renderhot.lut	
renderhsv.lut	
renderjet.lut	
rendersea.lut	
SPECTRUM.LUT	
surface.lut	
test.lut	
testlinear.lut	
X_hot.lut	
X_rain.lut	

9.13. Files in FRIEND/standard/

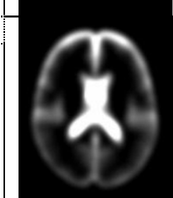
FRIEND/standard	FSL directory with standard templates.
avg152T1.nii.gz	
avg152T1_brain.nii.gz	
FMRIB58_FA_1mm.nii.gz	
FMRIB58_FA-skeleton_1mm.nii.gz	

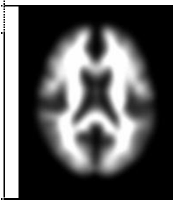
LowerCingulum_1mm.nii.gz	
MNI152_T1_0.5mm.nii.gz	
MNI152_T1_1mm_brain.nii.gz	
MNI152_T1_1mm_brain_mask.nii.gz	
MNI152_T1_1mm_first_brain_mask.nii.gz	
MNI152_T1_2mm.nii.gz	
MNI152_T1_2mm_b0.nii.gz	
MNI152_T1_2mm_brain.nii.gz	
MNI152_T1_2mm_brain_mask.nii.gz	

MNI152_T1_2mm_brain_mask_deweight_eyes.nii.gz	
MNI152_T1_2mm_brain_mask_dil.nii.gz	
MNI152_T1_2mm_edges.nii.gz	
MNI152_T1_2mm_eye_mask.nii.gz	
MNI152_T1_2mm_LR-masked.nii.gz	
MNI152_T1_2mm_skull.nii.gz	
MNI152_T1_2mm_strucseg.nii.gz	
MNI152_T1_2mm_strucseg_periph.nii.gz	
MNI152lin_T1_1mm.nii.gz	

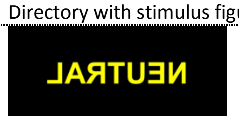
MNI152lin_T1_1mm_brain.nii.gz	
MNI152lin_T1_1mm_subbr_mask.nii.gz	
MNI152lin_T1_2mm.nii.gz	
MNI152lin_T1_2mm_brain.nii.gz	
MNI152lin_T1_2mm_brain_mask.nii.gz	

9.14. Files in FRIEND/standard/tissuepriors/

FRIEND/standard/tissuepriors	MNI152 standard space T1-weighted average structural template images.
avg152T1_brain.hdr avg152T1_brain.img	
avg152T1_csf.hdr avg152T1_csf.img	
avg152T1_gray.hdr	

avg152T1_gray.img	
avg152T1_white.hdr	
avg152T1_white.img	

9.15. Files in FRIEND/states/

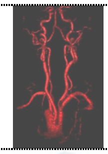
	Examples	Image inversion is only necessary when images are displayed to the participant through a mirror.
FRIEND/states		Directory with stimulus figures of cognitive or emotional states.
<condition1_figure>	neutral.jpg	
<condition2_figure>	pride.jpg	
....		....
<conditionn_figure>	tenderness.jpg	

9.16. Files in FRIEND/transferfunction/

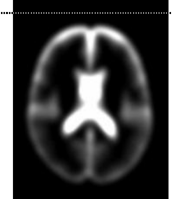
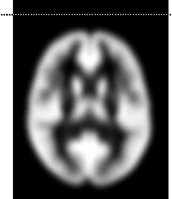
FRIEND/transferfunction	Opacity colormap files developed by IDOR Workgroup. An in-house file format was used. Each file is specific for a type of anatomical area.
Active Angio.tpf	
Active Bone (for Metallic Implant).tpf	
Active Bone.tpf	
Active CT.tpf	
Angio Aorta RM.tpf	
Bone (General).tpf	
Colon (Black Fat).tpf	
Colon (Color).tpf	
Colon (DCBE).tpf	
Coracao.tpf	
Coracao2.tpf	
CT Angio.tpf	
Lung (Solid).tpf	
Lung (Solid, Bone Visible).tpf	
Lung (Transparent).tpf	
Lung with Bone.tpf	
MR (High Range).tpf	
MR (Low Range).tpf	
MR (Med Range).tpf	
MR - angio abd + torax.tpf	
MR - angio abd.tpf	
MR - angio cranio.tpf	
MR - angio MMIIS.tpf	
MR - angio torax.tpf	
MR - angio.tpf	
MR- angio carotidas.tpf	
Muscle CT 2.tpf	
Muscle CT.tpf	

Muscle.tpf	
Skin.tpf	
Skin2.tpf	
Skull.tpf	

9.17. Files in FRIEND/transferfunction/images/

FRIEND/Templates/images	
angiocarotidas.bmp	
ct.bmp	
mr.bmp	

9.18. Files in FRIEND/tissuepriors/

FRIEND/tissuepriors	
avg152T1_brain.hdr avg152T1_brain.img	
avg152T1_csf.hdr avg152T1_csf.img	
avg152T1_gray.hdr avg152T1_gray.img	
avg152T1_white.hdr avg152T1_white.img	

10. DATA DIRECTORIES AND FILES

A basic configuration for the execution of FRIEND is described below. Both the reference anatomical image (RAI) and the reference functional images (RFI) must be present before beginning real-time processing. The description provided in this manual follows the dataset that is distributed with the software. However, FRIEND was designed in very flexible manner that and there's no need for any laboratory to change the organization method used.

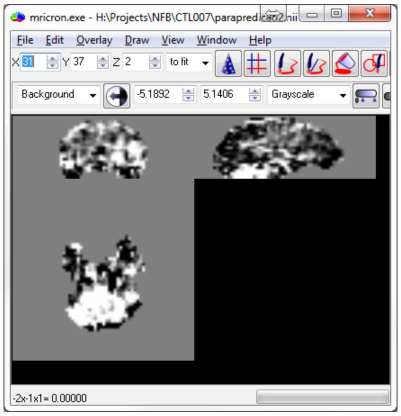
10.1. Directories and files in <study>/<subject>

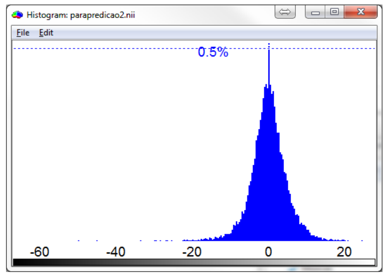
	Examples	Description
<study>	**Neurofeedback**	the study directory is the data root directory that must exist before running FRIEND
<subject>	**CTL0007**	A directory associated to a specific subject. The recommended (not mandatory) repository for <RAI>.nii and <RFI>.nii files that must exist before running FRIEND.
<run1> **.....** **<runx>**	**NFB01** **.....** **NFB04**	Directories where NIfTI files are stored after acquisition to be processed during the real-time pipeline.
<RAI> •	RAI.nii, CTL007MRI.nii	3D T1 anatomical reference image provided by the user. The image must exist before running FRIEND. Only NIfTI format file is accepted.
<RFI> •	RFI.nii, CTL007fMRI.nii	3D Functional reference image provided by user. Will be coregistered to <RAI>.nii to create a transformation matrix that will be used apply to functional images. The image must exist before running FRIEND. Only NIfTI format file is accepted.
<design1>.txt	DESIGN_NFB01.txt	Text files containing the experimental design of the study. An example is provided. More than one design file can be used.

After execution and depending on the number of runs a executed, a set of files and directories will be added to the subject directory. A fair description is given in the following table.

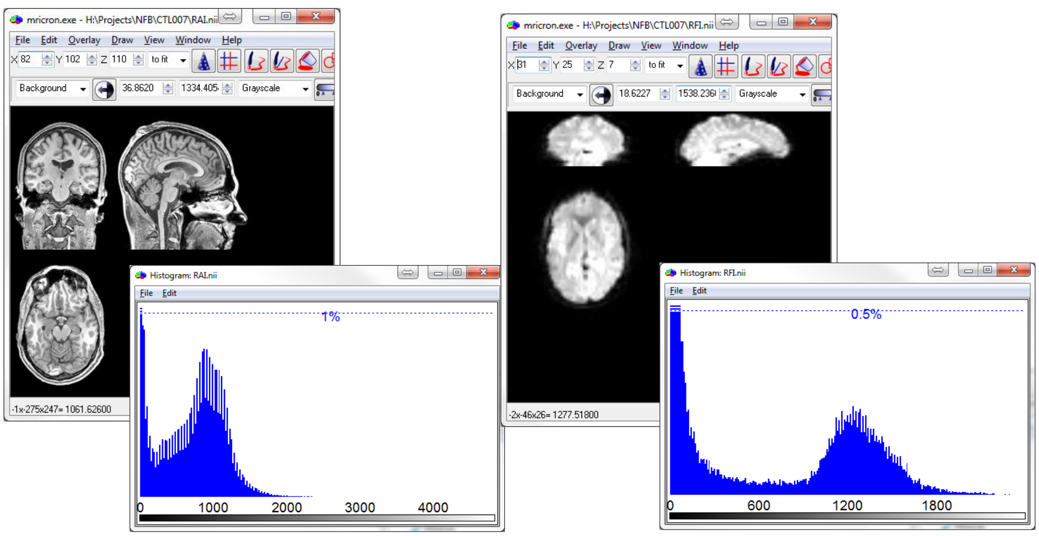
	Examples	Description
<study>	**Neurofeedback**	
<subject>	**CTL0007**	
<run1>	**NFB01**	
<run2>	**NFB02**	
.....	**.....**	
<runx>	**NFBx**	
glm		Contains files associated with the statistics processes of FRIEND.
input		Contains the resliced and skull stripped RAI and RFI images.
log		Contains the execution log, rotation, translation and root mean square parameters and .
preproc_<run1>		Contains rotation, translation and root mean square parameters for each real-time image acquired, and motion-corrected Gaussian smoothed images.
NIFTI		Contains the motion-corrected real-time images.
forprediction2.nii		RODRIGO
<RAI>	RAI.nii, CTL007MRI.nii	
<RFI>	RFI.nii, CTL007fMRI.nii	
study_params_<proc_type>_<crs>_<date><hour>	study_params_SVM_NFB01_20130921172932.txt	FRIEND configuration file with the last information used for run <crs>. The date and time of the execution is specified in the name of the file.
<design1>.txt	design_NFB01.txt	Text file containing the experimental design of the study.

10.1.1. forprediction2.nii file





10.1.2. Anatomical (RAI) and functional (RFI) reference image files



10.1.3. Study design file

1-15,NEUTRAL	During the acquisition of the first 15 scans, a figure with the word NEUTRAL in the name (ex: NEUTRAL.jpg, NEUTRAL,bmp, etc) from the FRIEND/States directory will be shown to the participant. If the Feedback option was selected on the input window of the FRIEND interface, figures on the FRIEND/Feedback/NEUTRAL directory will be used.
16-37,PRIDE	Idem for scans 16 to 37 and condition PRIDE
38-52,NEUTRAL	Idem for scans 38 to 52 and condition NEUTRAL
53-74,TENDERNESS	Idem for scans 53 to 74 and condition TENDERNESS
75-89,NEUTRAL	
90-111,TENDERNESS	
112-126,NEUTRAL	
127-148,PRIDE	
149-163,NEUTRAL	

164-185,PRIDE	
186-200,NEUTRAL	
201-222,TENDERNESS	
223-237,NEUTRAL	
238-259,TENDERNESS	
260-274,NEUTRAL	
275-296,PRIDE	

10.1.4. Study parameters file

[FRIEND]	
Subject=CTL007	Subject directory and subject identifier
RAI=c:\Projects\NEUROFEEDBACK\CTL007\RAI.nii	Reference Anatomical Image (RAI) is the image used to register functional images into native space.
RFI=c:\Projects\NEUROFEEDBACK\CTL007\RFI.nii	Reference Functional Image (RFI) is the functional image acquired offline (i.e., not during realtime acquisition). Any deformations to the RAI are performed with the RFI. Transformations are applied to images acquired during realtime to optimize and speed processing.
Prefix=c:\Projects\NEUROFEEDBACK\CTL007\NFB01\DRIN-	A string text containing the directory of realtime images and the prefix for filenames. Prefix for realtime image names (FRIEND reads Analyze, nifty and DICOM from Philips Achieva 3.0T and Siemens 7T VB17 in Oxford). After realtime images are acquired they are stored in a directory for retrieval and analysis. The software will use the prefix name to identify the images and read them in an orderly manner. For example, if the prefix is "DRIN-", the following filenames should appear in the directory: "DRIN-1.{hdr+img}, DRIN-2.{hdr+img}, DRIN-3.{hdr+img}and so on
Design=c:\Projects\NEUROFEEDBACK\DESIGN_NFB01.txt	Directory and filename of the design of the study describing how condition signs must be presented to the participant.
TR=2	Measured in seconds, the time of repetition or Repetition Time is the amount of time that passes between consecutive excitation pulses.
SlidingWindowSize=3	
FuncVolumes=296	Total number of volumes acrquired in the current functional run
StudyDir=c:\Projects\NEUROFEEDBACK	The study directory. FRIEND expects the subject directory to be inside the study directory. If it doesn't exist, FRIEND creates the directory. Be aware that RAI and RFI must be present in order to FRIEND execute griselda
BaselineCondition=NEUTRAL	Baseline condition with the same name used in the <design.txt> (ex: design_NFB01.txt) file.
Offset=4	Number of functional volumes discarded on each or at the beginning of the block to account for BOLD and/or cognitive delay
tTestCutOff=5.50	t-test map threshold used for feature selection
ClusterSize=3	Cluster size and threshold for t-test maps
ModelRunSuffix=NFB01	The suffix of a previous run that will be used as classifier.
CurrentRunSuffix=NFB02	Suffix for current run.
ByCutOff=1	ByCutOff is set to 1 if t-test maps wil be thresholded with the tTestCutOff and ClusterSize values. # If ByCutOff = 0, set percentile of voxels from t-test maps that will be included. O que acontece se ByCutOff . 1 e' 1. Qq outra coisa empty entao zero
KoushFiltering=0	
IncludeMotionParameters=0	Set to 1 to include 6 motion (translations and rotations) covariates into GLM model
ReferenceFirstVolSequence=0	Set to 0 to use RFI as the standard space for processing functional files. Set to 1 to use the first run volume instead. In this case, the final statistics files will be converted to the RFI standard space.
ConditionContrasts=0	Set to 1 to let the program create all combination of contrasts (without baseline)
AverageMeanOffset=0	# Number of volumes to be discarded from the baseline block condition before signal averaging, in order to perform mean subtraction (i.e., subtract each volume of a condition of interest from the baseline mean signal). The goal of using an offset is to reduce the contribution of a the previous block to the baseline signal average.
MNITemplate=	Standard MNI template.
MNIMask=	Mask of apriori regions for the study in MNI space
StimulusPresentationOffset=2	Delay (in scans) before starting neurofeedback stimulus presentation
PerformSUSAN=0	Set to 1 for FSL SUSAN noise reduction
Kernel3D=0	A 3x3x3 Gaussian box centered on the target voxel is used to obtain the mean activation

	for display as default. Set to 1 to use the same calculation method for prediction
GlobalIntensityNormalisation=0	Normalize volume intensity (akin to Grand mean scaling)
TrainingPercentage=0.50	Percentage of the run used for training
FWHM=5.00	FWHM kernel for Gaussian smoothing of functional images
LOOWeightThreshold=0.80	Weight threshold for Leave-One-Out SVM feature selection
LOOBestVoxelsPercentile=0.05	Percentile of voxels selected after Leave-One-Out SVM feature selection.
SVMFeatureSelection=0	Set to 1 use WeightThreshold and BestVoxelsPercentile
PercentileHigherVoxels=20.00	If ByCutOff = 0, set percentile of voxels from t-test maps that will be included
PerformNeurofeedback=1	Set to 1 to display neurofeedback figures correlated with the cognitive state of the subject
UseWholeSubjectSpaceMask=0	Set to 1 if you want to use all voxels contained in a MNISubjectMask as mask, (over-ride ByCutOff and PercentileHigherVoxels)
BrainThreshold=10.000	FSL MELODIC Brain/background threshold # Using point (.) or comma (,) depends on Windows Regional Settings
ReferenceWholeVolume=0	Set to 1 if PercentileHigherVoxels refers to the whole brain. Otherwise, PercentileHigherVoxels refers to TemplateMNI.
StorePredictions=0	Save the input volumes of the classification step for further analysis.
MaskForMeanExtraction=	
LowTValueVoxelsMask=	
ActivationLevelMask=	
ActivationLevelMaskReference=	
ActivationLevelMaskType=1	
TriggerActivationLevel=3	
ActivationLevelChange=0.25	
ActivationLevel=0.015	
FeedBackType=1	Type of feedback processing (1:SVM, 2: ROI, 3: functional connectivity)
RegionsFile=	
RegionsMapFile=	
CorrelationWindowsSize=10	
CorrelationMapFile=	
CorrelationMapFileRef=	
RegionExtractionMapFile=	
RegionExtractionMapPerc=20	
SufixNumberWidth=5	
InvX=0	
InvY=1	
InvZ=0	
MCType=1	
ActivationLevelAllowDownHill=1	

10.2. Files in <study>/<subject>/glm

	Examples	Description
<study>/<subject>/glm	Neurofeedback/CTL0007/glm	
4D_mc_ms_G_3sw_<crs>.nii •	4D_mc_ms_G_NFB01.txt	4D volume containing 3D motion-corrected , baseline mean subtracted, Gaussian-filtered, and N-slided window averaged images, where N is the <sliding_window_size> defined in the input window (Figure 7). The number of files is equal to the number of functional volumes (<functional_vols>) acquired during the study session. The 4D volume will be used in the classification phase.
betas_<crs>.nii •	betas_NFB01.txt	4D image file containing as many images as conditions in the current session (e.g: NEUTRAL, POSITIVE, NEGATIVE. See section Experiment Workflow Overview for more details.
confounds_<crs>.txt •	confounds_NFB01.txt	Translation and rotation parameters for all RTFI images (i.e. images acquired during real-time processing) in the current run
contrast_<crs>.txt •	contrast_NFB01.txt	Contrasts for the study. Can be provided by the user or created by FRIEND according to the value set in

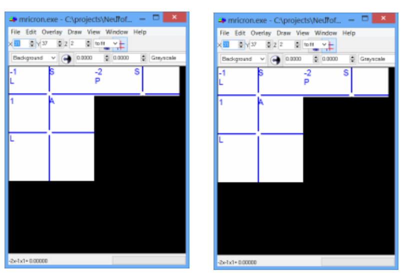
		ConditionContrasts in the study_params.txt file.
<subject>_<crs>.frf •	CTL0007_NFB01.frf	
<subject>_<crs>.fsf •	CTL0007_NFB01.fsf	
<subject>_<crs>. min •	CTL0007_NFB01.min	
<subject>_<crs>.ppm •	CTL0007_NFB01.ppm	
<subject>_<crs>.trg •	CTL0007_NFB01.trg	
<subject>_<crs>.cov_ppm •	CTL007_NFB01_cov.ppm	
design_with2Gamma_<crs>.txt •	design_with2Gamma_NFB01.txt	Design matrix after convolution with a 2-Gamma function
<condition_1>.txt • ..... <condition_n>.txt	neutral.txt pride.txt anger.txt	fMRI boxcar values for a specific condition. The name of the condition is extracted from the design text file.
pvalues_<crs>.nii •	pvalues_NFB01.nii	3D image file containing p-values associated with the Student t-test values in tstats_features_ALL_<crs>.nii.
tstats_features_ALL_<crs>.nii •	tstats_features_ALL_NFB01.nii	3D image containing the maximum Student t-tests value for each voxel in the 4D Student t-test image file associated with the defined contrasts
tstats_features_cut_off_<crs>.nii •	tstats_features_cut_off_NFB02.nii	3D image file created after thresholding the Student t-test 3D image file with a user-defined cut off value.
tstats_features_<crs>.nii •	tstats_features_NFB01.nii	A 3D image file created after thresholding tstats_features_cut_off_<crs>.nii with the <cluster_size> threshold.
tstats_features_<crs>_NoMasked.nii	tstats_features_NFB02_NoMasked.nii	
tstats_<crs>.nii •	tstats_NFB01.nii	4D image file containing Student t-tests values for all defined contrasts.

10.2.1. 4D_mc_ms_G_<crs>.nii file (ex: 4D_mc_ms_G_NFB01.nii)

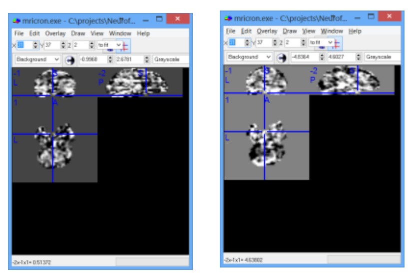
Volumes for depression study example:

Depression study

dataset



volumes 1 - 15

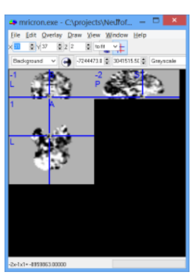


volumes 16 - 296

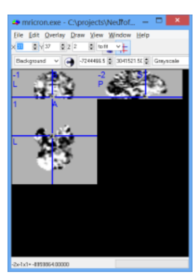
10.2.2. betas_<crs>.nii file (ex: betas_NFB01.nii)

Depression study

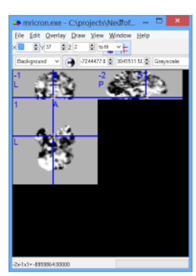
dataset



volume 1



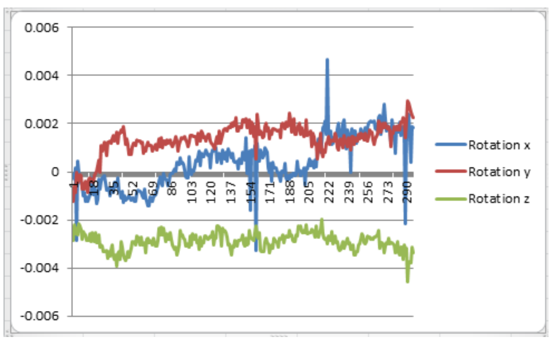
volume 2

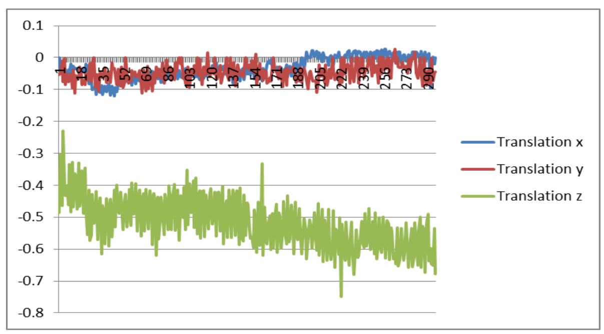


volume 3

10.2.3. confounds_<crs> (ex: confounds_NFB01)

Translation x	Translation y	Translation z	Rotation x	Rotation y	Rotation z
-0.00013255	-0.001235332	-0.00287383	-0.000779784	-0.054007102	-0.486807972
-0.000304182	-0.000583091	-0.002204041	-0.042439871	-0.049018707	-0.303667128
0.000155922	-0.000840255	-0.002584936	-0.011838699	-0.01110234	-0.464510351
-0.002860264	-8.47E-22	-0.002333147	-0.0311915	-0.076808088	-0.229665309
0.000458163	-0.000453595	-0.002629919	-0.033508923	-0.002735046	-0.395145953
-2.13E-05	-0.000288729	-0.002151035	-0.043250438	-0.084019348	-0.433373094
-0.0003131	-0.000124832	-0.002255452	-0.054785769	-0.051600162	-0.401895136
-0.000437088	-0.000155563	-0.002400876	-0.037439246	-0.076449424	-0.462187886
....	....	....	....	....	....
0.001777384	0.002091822	-0.003191572	0.012269082	-0.075640388	-0.637440443
0.00240757	0.002927239	-0.004573795	-0.096598007	-0.081845067	-0.596496046
0.002388119	0.002860937	-0.00372081	-0.035032041	-0.001358395	-0.646332383
0.000376254	0.002463332	-0.003782186	0.001662528	-0.073689722	-0.651738644
0.001858225	0.002342404	-0.003142863	-0.020106478	-0.047109194	-0.534774542
0.001855669	0.002272029	-0.00338386	0.001046023	-0.045528531	-0.677837849





10.2.4. contrast_<crs>.txt file (ex: contrast_NFB01)

/ContrastName1	""				
/ContrastName2	""				
/ContrastName3	""				
/ContrastName4	""				
/NumWaves	3				
/NumContrasts	4				
/PPheights	1.288462e+00	1.270643e+00	1.153068e+00	1.153068e+00	
/RequiredEffect	1.064	0.982	1.229	1.229	
/Matrix					
	-1.00E+00	1.00E+00	0.00E+00		
	-1.00E+00	0.00E+00	1.00E+00		
	0.00E+00	-1.00E+00	1.00E+00		
	0.00E+00	1.00E+00	-1.00E+00		

10.2.5. <subject>_<crs>.frf file (ex: CTL0007_NFB01.frf)

1	
2	
3	

10.2.6. <subject>_<crs>.fsf file (ex: CTL0007_NFB01.fsf)

# Analysis level	
# 1 : First-level analysis	
# 2 : Higher-level analysis	
set fmri(level) 1	
# TR(s)	
set fmri(tr) 2	
# Total volumes	
set fmri(npts) 296	
# Delete volumes	
set fmri(ndelete) 0	
# Critical z for design efficiency calculation	
set fmri(critical_z) 5.3	
# Noise level	
set fmri(noise) 0.66	
# Noise AR(1)	
set fmri(noisear) 0.34	
# Add motion parameters to model	
# 0 : No	
# 1 : Yes	
set fmri(motionevs) 0	
# Number of EVs	
set fmri(evs_orig) 3	
set fmri(evs_real) 3	
set fmri(evs_vox) 0	
# Number of contrasts	
set fmri(ncon_orig) 4	
set fmri(ncon_real) 4	
# Number of F-tests	
set fmri(nftests_orig) 0	
set fmri(nftests_real) 0	
# Highpass temporal filtering	
set fmri(temphp_yn) 1	
# Lowpass temporal filtering	
set fmri(templp_yn) 0	
# High pass filter cutoff	
set fmri(paradigm_hp) 100	

# EV 1 title	
set fmri(evtitle1) "NEUTRAL"	
# Basic waveform shape (EV 1)	
# 0 : Square	
# 1 : Sinusoid	
# 2 : Custom (1 entry per volume)	
# 3 : Custom (3 column format)	
# 4 : Interaction	
# 10 : Empty (all zeros)	
set fmri(shape1) 2	
# Convolution (EV 1)	
# 0 : None	
# 1 : Gaussian	
# 2 : Gamma	
# 3 : Double-Gamma HRF	
# 4 : Gamma basis functions	
# 5 : Sine basis functions	
# 6 : FIR basis functions	
set fmri(convolve1) 3	
# Convolve phase (EV 1)	
set fmri(convolve_phase1) 0	
# Apply temporal filtering (EV 1)	
set fmri(tempfilt_yn1) 1	
# Add temporal derivative (EV 1)	
set fmri(deriv_yn1) 0	
# Custom EV file (EV 1)	
set fmri(custom1) "C:\projects\NEUROFEEDBACK\CTL007\glm\NEUTRAL.txt"	
# Gamma sigma (EV 1)	
set fmri(gammasigma1) 3	
# Gamma delay (EV 1)	
set fmri(gammadelay1) 6	
# Orthogonalise EV 1 wrt EV 0	
set fmri(ortho1.0) 0	
# Orthogonalise EV 1 wrt EV 1	
set fmri(ortho1.1) 0	
# Orthogonalise EV 1 wrt EV 2	
set fmri(ortho1.2) 0	
# Orthogonalise EV 1 wrt EV 3	
set fmri(ortho1.3) 0	
# EV 2 title	
set fmri(evtitle2) "PRIDE"	
# Basic waveform shape (EV 2)	
# 0 : Square	
# 1 : Sinusoid	
# 2 : Custom (1 entry per volume)	
# 3 : Custom (3 column format)	

# 4 : Interaction	
# 10 : Empty (all zeros)	
set fmri(shape2) 2	
# Convolution (EV 2)	
# 0 : None	
# 1 : Gaussian	
# 2 : Gamma	
# 3 : Double-Gamma HRF	
# 4 : Gamma basis functions	
# 5 : Sine basis functions	
# 6 : FIR basis functions	
set fmri(convolve2) 3	
# Convolve phase (EV 2)	
set fmri(convolve_phase2) 0	
# Apply temporal filtering (EV 2)	
set fmri(tempfilt_yn2) 1	
# Add temporal derivative (EV 2)	
set fmri(deriv_yn2) 0	
# Custom EV file (EV 2)	
set fmri(custom2) "C:\projects\NEUROFEEDBACK\CTL007\glm\PRIDE.txt"	
# Gamma sigma (EV 2)	
set fmri(gammasigma2) 3	
# Gamma delay (EV 2)	
set fmri(gammadelay2) 6	
# Orthogonalise EV 2 wrt EV 0	
set fmri(ortho2.0) 0	
# Orthogonalise EV 2 wrt EV 1	
set fmri(ortho2.1) 0	
# Orthogonalise EV 2 wrt EV 2	
set fmri(ortho2.2) 0	
# Orthogonalise EV 2 wrt EV 3	
set fmri(ortho2.3) 0	
# EV 3 title	
set fmri(evtitle3) "TENDERNESS"	
# Basic waveform shape (EV 3)	
# 0 : Square	
# 1 : Sinusoid	
# 2 : Custom (1 entry per volume)	
# 3 : Custom (3 column format)	
# 4 : Interaction	
# 10 : Empty (all zeros)	
set fmri(shape3) 2	
# Convolution (EV 3)	
# 0 : None	
# 1 : Gaussian	
# 2 : Gamma	

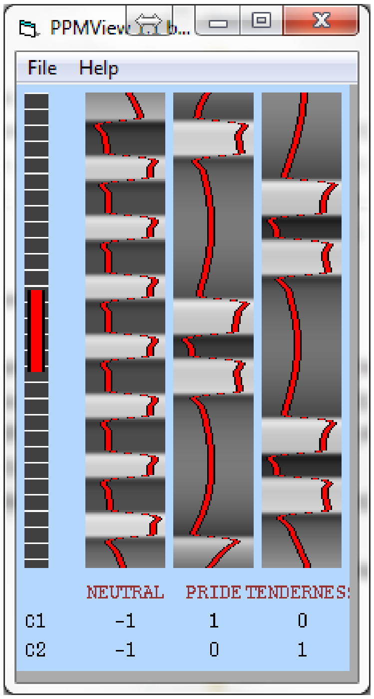
# 3 : Double-Gamma HRF	
# 4 : Gamma basis functions	
# 5 : Sine basis functions	
# 6 : FIR basis functions	
set fmri(convolve3) 3	
# Convolve phase (EV 3)	
set fmri(convolve_phase3) 0	
# Apply temporal filtering (EV 3)	
set fmri(tempfilt_yn3) 1	
# Add temporal derivative (EV 3)	
set fmri(deriv_yn3) 0	
# Custom EV file (EV 3)	
set fmri(custom3) "C:\projects\NEUROFEEDBACK\CTL007\glm\TENDERNESS.txt"	
# Gamma sigma (EV 3)	
set fmri(gammasigma3) 3	
# Gamma delay (EV 3)	
set fmri(gammadelay3) 6	
# Orthogonalise EV 3 wrt EV 0	
set fmri(ortho3.0) 0	
# Orthogonalise EV 3 wrt EV 1	
set fmri(ortho3.1) 0	
# Orthogonalise EV 3 wrt EV 2	
set fmri(ortho3.2) 0	
# Orthogonalise EV 3 wrt EV 3	
set fmri(ortho3.3) 0	
# Contrast & F-tests mode	
# real : control real EVs	
# orig : control original EVs	
set fmri(con_mode_old) orig	
set fmri(con_mode) orig	
# Display images for contrast_real 1	
set fmri(conpic_real.1) 1	
# Title for contrast_real 1	
set fmri(conname_real.1) ""	
# Real contrast_real vector 1 element 1	
set fmri(con_real1.1) -1.00	
# Real contrast_real vector 1 element 2	
set fmri(con_real1.2) 1.00	
# Real contrast_real vector 1 element 3	
set fmri(con_real1.3) 0.00	
# Display images for contrast_real 2	
set fmri(conpic_real.2) 1	

# Title for contrast_real 2	
set fmri(conname_real.2) ""	
# Real contrast_real vector 2 element 1	
set fmri(con_real2.1) -1.00	
# Real contrast_real vector 2 element 2	
set fmri(con_real2.2) 0.00	
# Real contrast_real vector 2 element 3	
set fmri(con_real2.3) 1.00	
# Display images for contrast_real 3	
set fmri(conpic_real.3) 1	
# Title for contrast_real 3	
set fmri(conname_real.3) ""	
# Real contrast_real vector 3 element 1	
set fmri(con_real3.1) 0.00	
# Real contrast_real vector 3 element 2	
set fmri(con_real3.2) -1.00	
# Real contrast_real vector 3 element 3	
set fmri(con_real3.3) 1.00	
# Display images for contrast_real 4	
set fmri(conpic_real.4) 1	
# Title for contrast_real 4	
set fmri(conname_real.4) ""	
# Real contrast_real vector 4 element 1	
set fmri(con_real4.1) 0.00	
# Real contrast_real vector 4 element 2	
set fmri(con_real4.2) 1.00	
# Real contrast_real vector 4 element 3	
set fmri(con_real4.3) -1.00	

10.2.7. <subject>_<crs>.min file (ex: CTL0007_NFB01.min)

1	

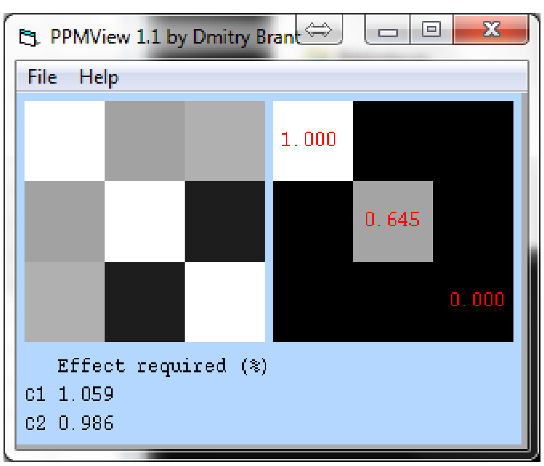
10.2.8. <subject>_<crs>.ppm file (ex: CTL0007_NFB01.ppm)



10.2.9. <subject>_<crs>.trg file (ex: CTL0007_NFB01.trg)

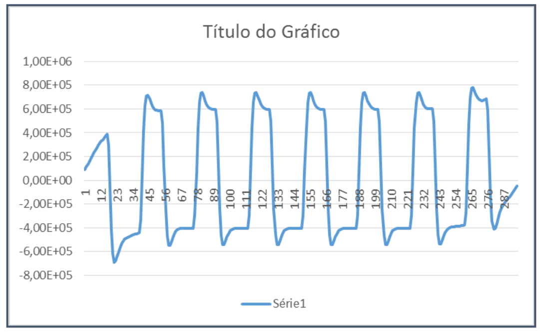
-5.00E-01	3.65E+01	7.35E+01	1.11E+02	1.48E+02	1.85E+02	2.22E+02	2.59E+02	33	
1.45E+01	1.26E+02	1.63E+02	2.74E+02	40					
5.15E+01	8.85E+01	2.00E+02	2.37E+02	40					

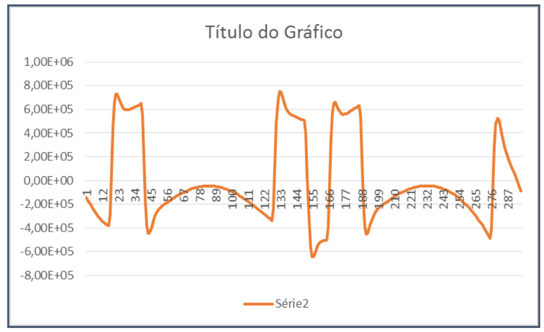
10.2.10. <subject>_<crs>_cov.ppm file (ex: CTL0007_NFB01_cov.ppm)

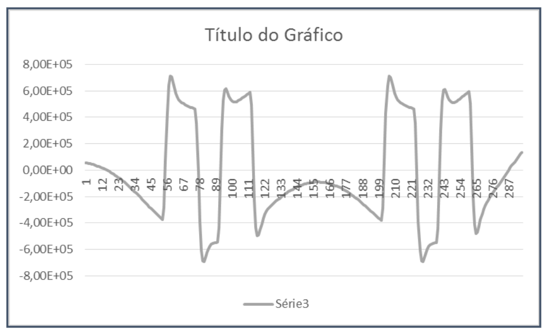


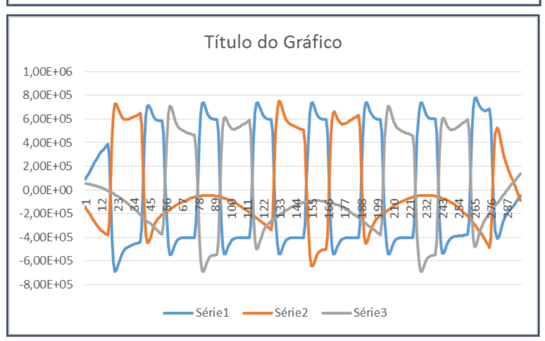
10.2.11. design_with2Gamma_<crs>.txt file (ex: design_with3Gamma_NFB01.txt)

/NumWaves 3			
/NumPoints 296			
/PPheights	1.279210e+000	1.279210e+000	1.279210e+000
/Matrix			
8.765430e-002	-1.411721e-001	5.351777e-002	
1.132160e-001	-1.654226e-001	5.220668e-002	
1.383391e-001	-1.885025e-001	5.016334e-002	
1.627896e-001	-2.104110e-001	4.762135e-002	
1.864058e-001	-2.311484e-001	4.474266e-002	
2.091187e-001	-2.507167e-001	4.159806e-002	
2.309130e-001	-2.691192e-001	3.820614e-002	
2.517989e-001	-2.863602e-001	3.456129e-002	
....			
-1.835484e-001	1.684169e-001	1.513149e-002	
-1.678870e-001	1.368823e-001	3.100465e-002	
-1.522338e-001	1.055270e-001	4.670678e-002	
-1.361699e-001	7.395795e-002	6.221194e-002	
-1.195157e-001	4.202097e-002	7.749478e-002	
-1.022041e-001	9.673883e-003	9.253026e-002	
-8.419746e-002	-2.309633e-002	1.072938e-001	
-6.547960e-002	-5.628136e-002	1.217610e-001	
-4.604551e-002	-8.986229e-002	1.359078e-001	



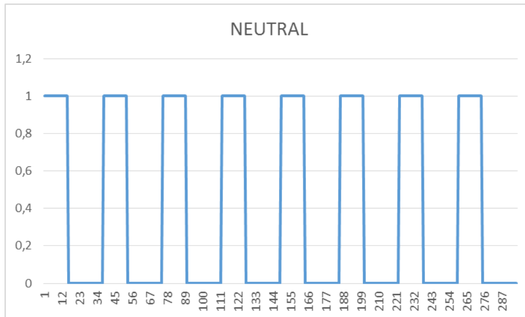


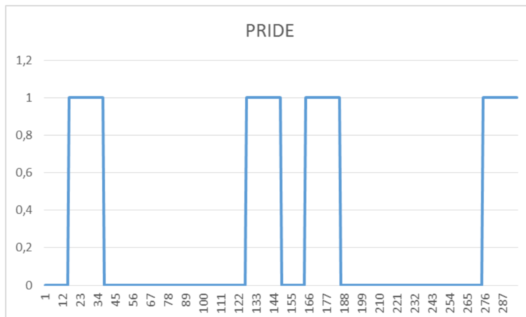


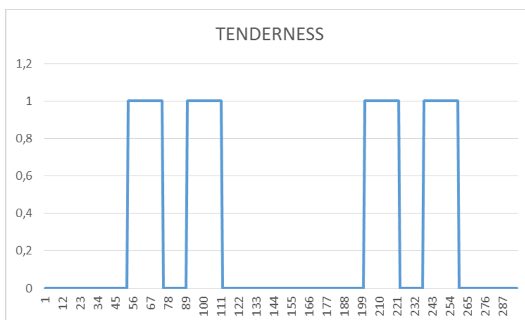


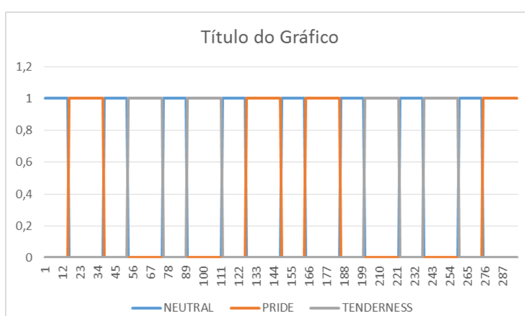
10.2.12. <condition> file (ex: NEUTRAL, PRIDE, TENDERNESS)

NEUTRAL	PRIDE	TENDERNESS
1	0	0
1	0	0
…	…	…
0	1	0
0	1	0
0	1	0
…	…	…
1	0	0
1	0	0
1	0	0
…	…	…
0	0	1
0	0	1
0	0	1
…	…	…
1	0	0
1	0	0
1	0	0
…	…	…
1	0	0
1	0	0
1	0	0

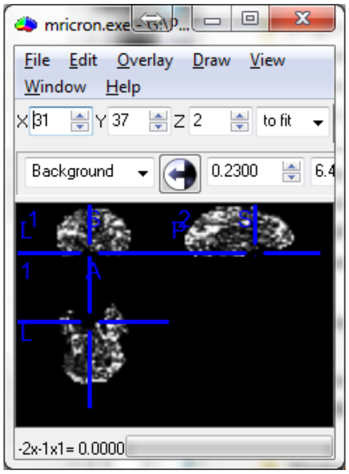


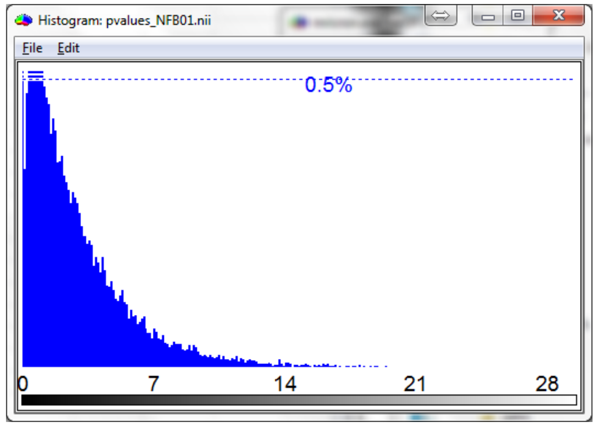




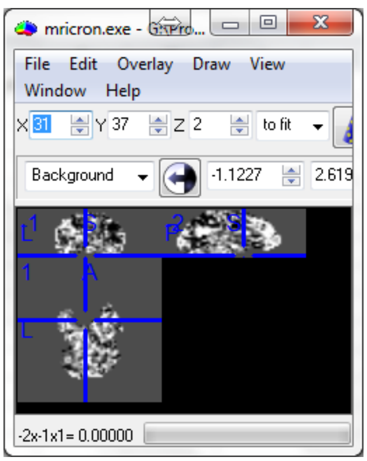


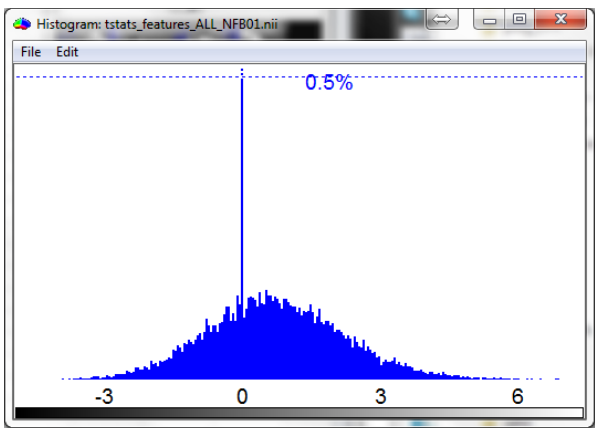
10.2.13. tstats_<crs> file (ex: tstats_NFB01)



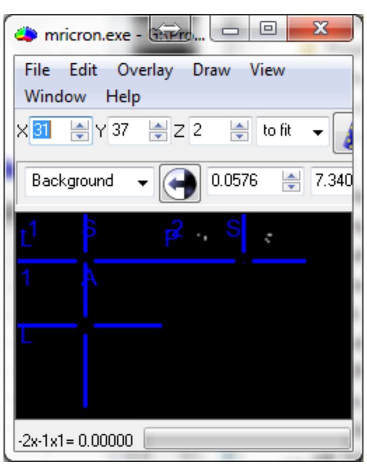


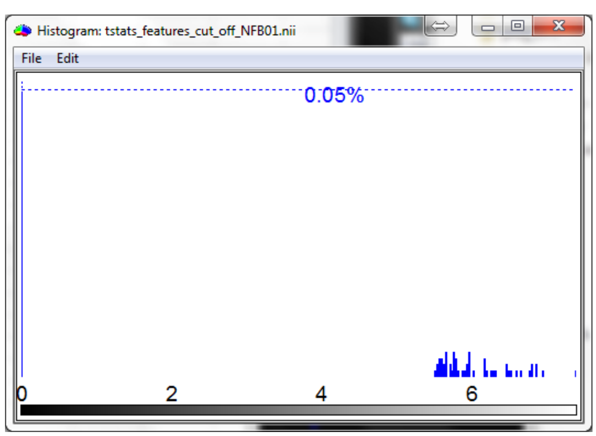
10.2.14. tstats_features_ALL_<crs> file (ex: tstats_features_ALL_NFB01)



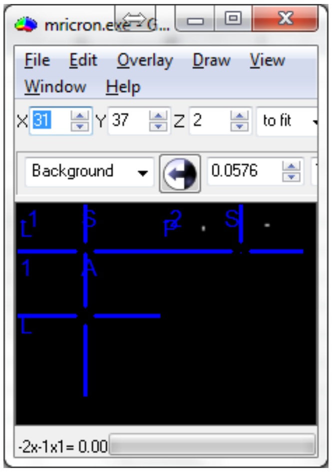


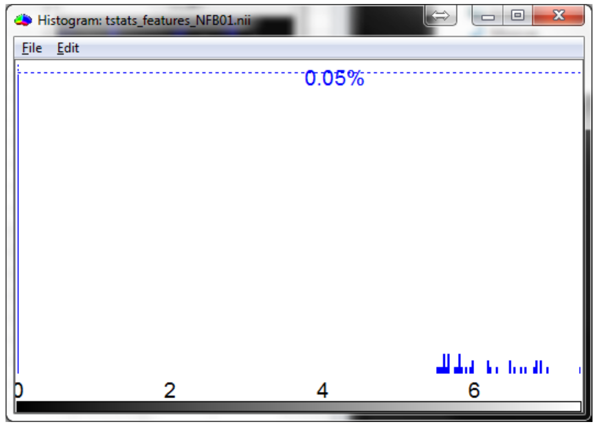
10.2.15. tstats_features_cut_off_<crs> file (ex: tstats_features_ALL_NFB01)



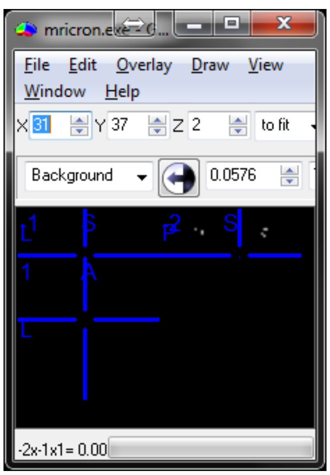


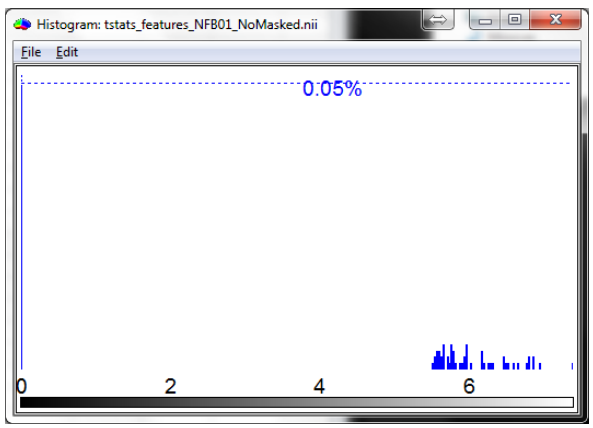
10.2.16. tstats_features_<crs> file (ex: tstats_features_NFB01)



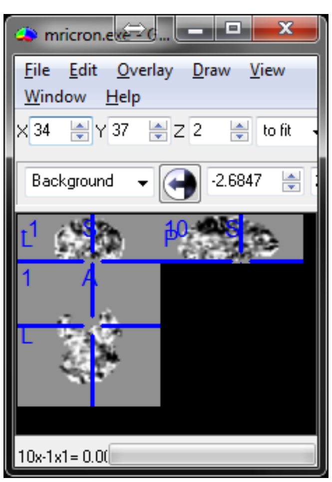


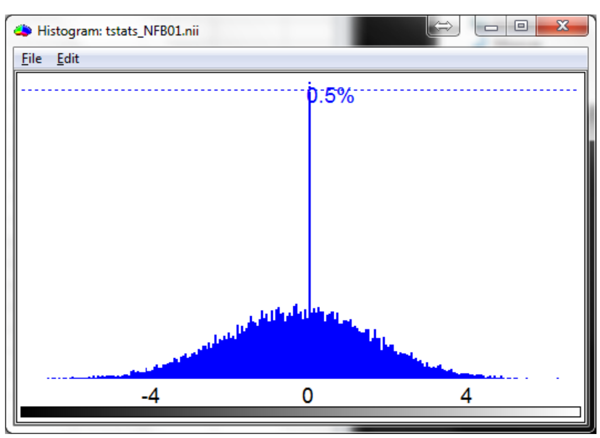
10.2.17. tstats_features_<crs>_NoMasked file (ex: tstats_features_NFB01_NoMasked)





10.2.18. tstats_<crs> file (ex: tstats_NFB01)





10.3. Files in <study>/<subject>/input

	Description
<study>/<subject>/input	
RAI_ax.nii •	If the <RAI>.nii provided by the user is not in axial orientation, the image is transversally sliced., as FSL routines work with images in axial orientation only. Brain volumes acquired differently must be reoriented.
RAI_ax_cube.nii •	For better performance of the FSL skull stripping algorithm (BET) the RAI_ax.nii must be resampled to create an image with isotropic dimensions (i.e. the same number of rows, columns and slices).
RAI_ax_cube_sks.nii	
RAI_ax_cube_sks_overlay.nii	
RAI_ax_cube_sks_rspl2RFI.nii •	To speed up registration between different image modalities, the high-resolution image (RAI_ax_cube_sks.nii) image is resampled to the low-resolution reference image (<RFI>.nii) .
RFI2RAI_ax_cube_sks.mat •	Deformation coregistration parameters from RFI to RAI_ax_cube_sks.nii (reference). The corresponding transformation matrix is applied to the activation maps for the display results.
RFI_binmask.nii •	Binary mask derived from <RFI>.nii
RFI_sks.nii •	The result of skull stripping <RFI>.nii
RFI_sks_overlay.nii	

10.4. Files in <study>/<subject>/log

<study>/<subject>/log	Neurofeedback/CTL007/log	
confounds_<crs>.txt	confounds_NFB01.txt	
logfile_<crs>.txt	logfile_NFB01.txt	
rms_abs_<crs>.rms	rms_abs_NFB01.rms	
rms_<crs>.png	rms_NFB01.png	
rot_<crs>.png	rot_NFB01.png	
trans_<crs>.png	trans_NFB01.png	

10.5. Files and directories in <study>/<subject>/preproc_<crs>

<study>/<subject>/preproc_<crs>	Neurofeedback/CTL0007/preproc_NFB01	Directory containing preprocessed images for a specific run.
NIFTI		Directory containing the motion-corrected real-time images
<nifti>.mat	DRIN-00001.mat	Matrix with registration deformation parameters
<nifti>.par	DRIN-00001.par	
<nifti>.rms	DRIN-00001.rms	
<nifti>_abs_mean.rms	DRIN-00001_abs_mean.rms	
<nifti>_mc.nii	DRIN-00001_mc.nii	
<nifti>_mc_g.nii	DRIN-00001_mc_g.nii	

10.6. Files in <study>/<subject>/svm

<study>/<subject>/svm	Neurofeedback/CTL0007/svm	Directory containing preprocessed images for a specific run.
	CTL007_NFB01.map	
	CTL007_NFB01.model	
	CTL007_NFB01.nii	
	CTL007_NFB01_wv.nii	
	training_NFB01.txt	
	training_result_NFB01.txt	

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1. TROUBLESHOOTING

FRIEND doesn't execute

If the FRIEND input window doesn't appear after trying to execute FRIEND, check if any dead process is active in the task manager and delete it as shown in Figure 11.

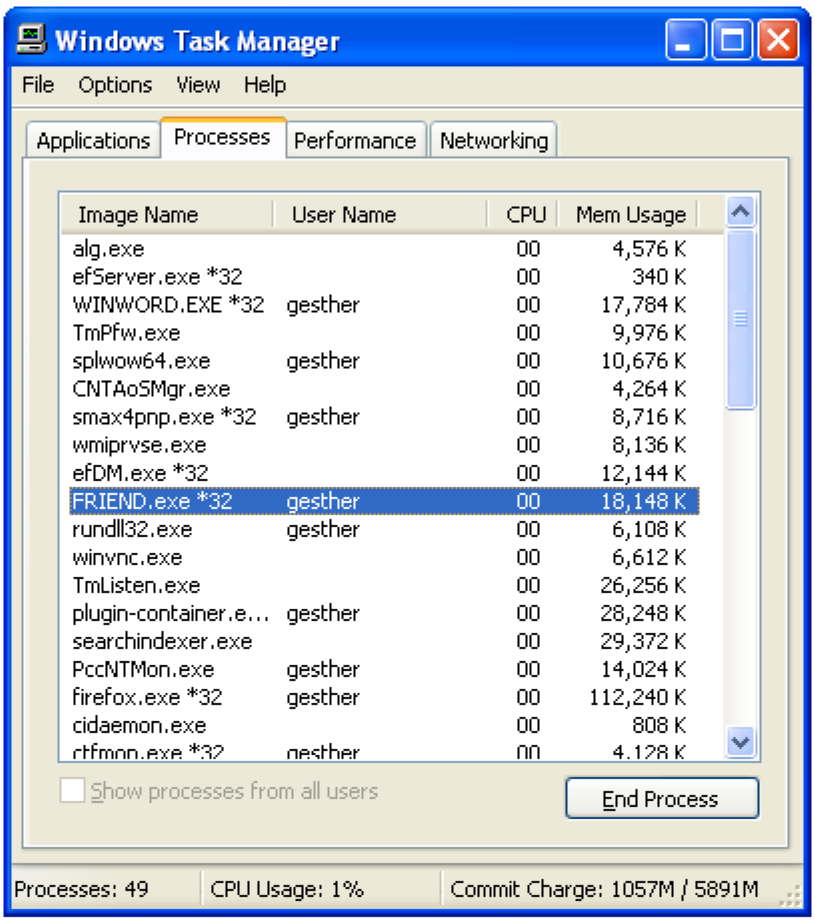

Figure 11. Task manager interface.

APPENDIX A. FSL WINDOWS® LIBRARY COMMANDS •

The FSL Windows® Library calls routines implemented within the FMRIB Software Library (FSL, http://www.fmrib.ox.ac.uk/fsl/). Each command was implemented as a function where the only parameter is the specific FSL command aimed to be executed. For example, the flirt command line is translated to: *flirt("flirt -in invol -ref refvol -out outvol -omat invol2refvol.mat -dof 6").* The approach will make migration to Linux straightforward in the future.

FSL library functions called within the FRIEND software were tested extensively. Other FSL library functions are undergoing tests. Some minor functions that serve solely to expose some inner features of the internal objects of the FSL library, like resample, demeaning, convolution and mean calculation were implemented in a separate file.

extern "C" __declspec(dllimport) int _stdcall fsl_glm(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall film_gls(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall fslroi(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall flirt(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall mcflirt(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall fslmerge(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall fslsplit(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall applywarp(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall applyxfm4D(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall bet(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall cluster(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall connectedcomp(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall convert_xfm(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall convertwarp(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall createlut(char *CmdLn);

extern "C" __declspec(dllimport) int _stdcall fnirt(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall fsl_boxplot(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall fsl_histogram(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall fsl_tsplot(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall fslcc(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall fslchfiletype(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall fslcomplex(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall fslcorrecthd(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall fslcpgeom(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall fslfft(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall fslhd(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall fslmaths(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall fslmeants(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall fslorient(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall fslstats(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall fslswapdim(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall fslcreatehd(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall fugue(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall fast(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall melodic(char *CmdLn); †
extern "C" __declspec(dllimport) int _stdcall overlay(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall slicer(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall slicetimer(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall smoothest(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall susan(char *CmdLn);
extern "C" __declspec(dllimport) int _stdcall feat_model(char *CmdLn);