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SVT OVERVIEW

The SVT software is a tool for determining the statistically significant regions of activation in single or multi-subject human brain functional studies. It can be also applied to structural brain data for analyzing developmental, dementia and other changes of anatomy over time.

All routines are invoked as standard UNIX commands and neither expect nor allow user interaction once the command has been issued. The series of 'C' subroutines which comprise the SVT library can be easily incorporated into the user's site specific programs adapted to their particular needs.

SVT includes a graphical user interface (GUI) written in Tcl/Tk for use on SGI machines. The user, however, needs to re-link, edit and revise the "*.c++" files, especially the system calls within them, because it is currently set up to work in the LONI's UNIX directory framework.

Currently, the SVT package does not provide any graphics or image display capabilities, however, if the user has MNI's "Display" and "register" (display ftp) packages the GUI for SVT allows the use of these fine visualization tools. Some file format converters are included in this software and interactive calls to "minc2raw" and "raw2minc" (ftp minc package) are employed by the SVT GUI. All of the input files are supposed to have been pre-registered (e.g., AIR) volumetric 1 byte per pixel data sets of size 181x217y181z, so that they fit within the common anatomical reference space and the associated probabilistic atlas. However, if the SVT GUI is used than the user is walked through the entire procedure step-by-step, from flipping and inverting (when necessary) the raw data through volumetric registration, intensity normalization, statistical analysis (SVT), and visualization of the results (Display/register). Quantitative goodness of warp evaluation is recommended prior to executing the SVT routines (e.g., WAIR). A collection of batch files and shell script are provided for incorporating the SVT software within the framework of the AIR and MINC environments. These include preprocessing, warping and file-format converting scripts.

This package was originally developed to work on Sun SPARC and SGI stations using the 'C' language compiler provided by Sun/SGI as part of the standard system software. If you currently use an 8 bits/pixel file format on a Sun SPARC station equipped with the standard 'C' compiler, have at least (XX Bytes + 16 MB) of RAM (where XX = (Number of data sets) *181*217*181 Bytes), and are familiar with the UNIX operating system, you should be able to install and use the SVT package without additional assistance, even if you

know nothing about 'C' programming. However, if any of these conditions is not met, it is likely that you will need the assistance of a 'C' programmer who is familiar with the UNIX operating system.

INSTALLATION AND COMPILING

1. change the working directory to SVT5_2.dir
2. type chmod +x MAKE2.com
3. type MAKE2.com

PROGRAM SYNOPSIS

For SGI users we recommend you try to install the graphical user interface (GUI) which tremendously simplifies the software. It also allows linking the SVT, AIR (polynomial warping) and MNI's "Display" and "register" (visualization tools) (display ftp) softwares.

There are two main routines in the SVT package. The first one, **SVT_MNI9_5_2_SS_flt**, is employed for analyzing activation versus rest functional volumes for single subject (SS) studies. It will generate and SVT image containing all: the positively and negatively statistically significant variations between the two functional volumes, and an outline of the probabilistic sub-volume partitioning (see **technical notes**).

The second statistical analysis program included in SVT has two versions **SVT_MNI9_5_2_MS_flt** and **SVT_MNI9_4_2_MS_flt**, and is geared toward the same type of analysis for determining the statistically significant regions of activation in functional brain data, however, it is applied to multi-subject (MS) and group studies. For example, if a group of patients are scanned under two different paradigms (usually referred to as "A(ctive)" and "R(est)" states), and we are interested in determining and locating the metabolic differences and perfusion between these two stimuli based on the group of data we use **SVT_MNI9_5_2_MS_flt** or **SVT_MNI9_4_2_MS_flt**. There are some differences in the level of statistical significance applied in the two versions, see **technical notes**.

Recently we have added some variations to the SVT_5_2, mainly differing by the methods used to correct for multiple testing. These include: **SVT_MNI9_5_3_MS_flt**, allows the user to explicitly specify the FWHM in the range [0.1, 19.9] mm, with a stepsize of 0.1 mm; **SVT_simple_MS_flt** and **SVT_simple_SS_flt**, where there's no correction for multiple testing; and **bootstrap_SVT**, a new bootstrap approach for correcting the threshold levels for large number of statistical tests.

In addition, several pre- and post-processing procedures are supplied to ease the data registration (**flipMy3D_1**), intensity distribution (**histogram**), obtaining ROI statistics (**get_MNI_ROI_info**) and (**mean_var_bin1**), intensity normalization (**interSubj_normROI1** and **intraSubj_normPutamen**) and interpretation of the results (see various "batch" files). A number of batch files and shell scripts are also included to help with running SVT (batch_SVT_MS, batch_SVT_SS), registering the data using **AIR** (batch_warp, batch_makeaheader) and converting and visualizing the data and the results using **MNI**'s **MINC** data format and their **display** package.

ROUTINES

- **SVT_MNI9_5_2_SS_flt**

  Purpose:
  This SVT command is used to statistically analyze the variations between two human brain functional volumes obtained under different stimulation paradigms.

  You need to have the two stereotactic data sets pre-processed according to the “Techniques” section of this document. The output SVT volumes are 4 bytes per pixel (floating point) stereotactic images of size 181x217y181z. Intensities are positive and represent the Z-scores of statistical significance of the difference image.

  Usage:
  SVT_MNI9_5_2_SS_flt *A_postprocessed.img R_postprocessed.img Prob_Atlas.img SVT_SS_Pos.img SVT_SS_Neg.img*

  where the following definitions are used:

  A_postprocessed.img
  The A(ctivation) state is warped in T.img space (A_2_T.img).

  R_postprocessed.img
  The R(est) state is warped in T.img space (R_2_T.img)

  Prob_Atlas.img
  The name of the file containing the probabilistic Atlas (lobes5_diff_intensLikeAve1.img)

  SVT_SS_Pos.img and *SVT_SS_Neg.img*
  The positive and negative statistically significant images, as output of the SVT analysis.

  Examples:
  ./SVT_MNI9_5_2_SS_flt ./Act_After_Warp_2_avgedit_linWp12p.img ./Rest_After_Warp_avgedit_linWp12p.img ./lobes5_diff_intensLikeAve1.img ./Act_Rest_SVT_SS_Pos.img ./Act_Rest_SVT_SS_Neg.img

  This will save the 2D Discrete Wavelet transform of "4Bmri_0fltr.img" in the file "WT4Bmri_0fltr.img". Both files will contain 2D floating point (4 Bytes) images of size 256*256. Daubechies 20 coefficient filter bank is employed to find the DWT of the data. Also look at the batch file "batch_DWT_IWT".

- **SVT_MNI9_4_2_MS_flt** and **SVT_MNI9_5_2_MS_flt**

  Purpose:
  This SVT command is used to statistically analyze the variations between groups of human brain functional volumes obtained under different stimulation paradigms.

  You need to have all stereotactic data sets pre-processed according to the multi-subject part of

the “Techniques” section of this document. The output SVT volumes are 4 byte (floating point) per pixel stereotactic images of size 181x217y181z. The first image contains the positive and the second contains the negatively statistically significant voxels. Intensities of both SVT output images are in the range [0, infinity] and represent the exact Z-scores.

Usage:
SVT_MNI9_4_2_MS_flt *Num_Files1grp A_1_Wp_2_T.img ... [[A_k_Wp_2_T.img]] R_1_Wp_2_T.img ... [[R_k_Wp_2_T.img]] SVT_MS_Pos.img SVT_MS_Neg.img*

where the following definitions are used:

Num_Files1grp
the number of volumes in one group (the two groups have an equal number of data sets

A_1_Wp_2_T.img
A(ctivation) paradigm data for subject 1, warped in T.img space

A_k_Wp_2_T.img
A(ctivation) paradigm data for subject **k**, warped in T.img space, 1<=**k**<=Num_Files1grp

R_1_Wp_2_T.img
R(est) paradigm data for subject 1, warped in T.img space

R_k_Wp_2_T.img
R(est) paradigm data for subject **k**, warped in T.img space, 1<=**k**<=Num_Files1grp

Prob_Atlas.img
The name of the file containing the probabilistic Atlas (lobes9_diff_intens.img)

SVT_MS_Pos.img and *SVT_MS_Neg.img*
The files where the (positive and negative) output of the multi-subject (MS) SVT statistical analysis will be saved

Examples:
./SVT_MNI9_4_2_MS_flt Num_Files1grp ./A(1)Wp.img ... ./A(Num_Files1grp)Wp.img ./R(1)Wp.img ... ./R(Num_Files1grp)Wp.img ../lobes9_diff_intens.img ./A_R_SVT_MS_Pos.img ./A_R_SVT_MS_Neg.img

This command will use the post-processed groups of data (A's and R's are warped directly to the template, "avgedit.img") and the probabilistic partitioning information contained in "lobes9_diff_intens.img" to generate two multi-subject SVT output volumes (A_R_SVT_MS_Pos.img & A_R_SVT_MS_Neg.img) of the statistically significant differences between the two groups. Also look at the batch file "batch_SVT_MS". **Note** that the above example represents a **single** UNIX command-line.

- **SVT_MNI9_5_3_MS_flt**

  Purpose:
  This SVT command is used to statistically analyze the variations between groups of human brain functional volumes obtained under different stimulation paradigms.

  You need to have all stereotactic data sets pre-processed according to the multi-subject part of the “Techniques” section of this document. The output SVT volumes are 4 byte (floating point) per pixel stereotactic images of size 181x217y181z. The first image contains the positive and the second contains the negatively statistically significant voxels. Intensities of both SVT output images are in the range [0, infinity] and represent the exact Z-scores.

  Usage:
  SVT_MNI9_5_3_MS_flt *FWHM Num_Files1grp A_1_Wp_2_T.img ... [[A_k_Wp_2_T.img]] R_1_Wp_2_T.img ... [[R_k_Wp_2_T.img]] SVT_MS_Pos.img SVT_MS_Neg.img*

  Usually we refer to the first paradigm as A (activation) and the second one as R (rest). Let A.img and R.img be the two volumes we are analyzing and let T.img be our anatomical reference (template, "avgedit.img"). We denote by A_2_R.img the warped-and-resliced (using any algorithm) A.img in R.img space. There are at least 3 different ways one can transform A.img and R.img in T.img space, see “Techniques” section of this document.

  where the following definitions are used:

  FWHM
  The Full-Width-at-Half-Maximum (FWHM), e.g., 6.0, in the range [0.1;19.9] mm

  Num_Files1grp
  the number of volumes in one group (the two groups have an equal number of data sets

  A_1_Wp_2_T.img
  A(ctivation) paradigm data for subject 1, warped in T.img space

  A_k_Wp_2_T.img
  A(ctivation) paradigm data for subject **k**, warped in T.img space, 1<=**k**<=Num_Files1grp

  R_1_Wp_2_T.img
  R(est) paradigm data for subject 1, warped in T.img space

  R_k_Wp_2_T.img
  R(est) paradigm data for subject **k**, warped in T.img space, 1<=**k**<=Num_Files1grp

  Prob_Atlas.img
  The name of the file containing the probabilistic Atlas (lobes9_diff_intens.img)

  SVT_MS_Pos.img and *SVT_MS_Neg.img*

The files where the (positive and negative) output of the multi-subject (MS) SVT statistical analysis will be saved

Examples:
./SVT_MNI9_5_3_MS_flt 6.0 Num_Files1grp ./A(1)Wp.img ... ./A(Num_Files1grp)Wp.img ./R(1)Wp.img ... ./R(Num_Files1grp)Wp.img ../lobes9_diff_intens.img ./A_R_SVT_MS_Pos.img ./A_R_SVT_MS_Neg.img

This command will use the post-processed groups of data (A's and R's are warped directly to the template, "avgedit.img", ICBM space) and the probabilistic partitioning information contained in "lobes9_diff_intens.img" to generate two multi-subject SVT output volumes (A_R_SVT_MS_Pos.img & A_R_SVT_MS_Neg.img) of the statistically significant differences between the two groups. Also look at the batch file "batch_SVT_MS". The FWHM is 6.0 mm. **Note** that the above example represents a **single** UNIX command-line.

- **SVT_simple_MS_flt**

Purpose:
This SVT command is used to statistically analyze the variations between groups of human brain functional volumes obtained under different stimulation paradigms. **NO** correction for multiple testing is done in this routine. The user is encouraged to apply **bootstrap_SVT** following **SVT_simple_MS_flt** to get sensible results.

You need to have all stereotactic data sets pre-processed according to the multi-subject part of the “Techniques” section of this document. The output SVT volumes are 4 byte (floating point) per pixel stereotactic images of size 181x217y181z. The first image contains the positive and the second contains the negatively statistically significant voxels. Intensities of both SVT output images are in the range [0, infinity] and represent the exact Z-scores.

Usage:
SVT_simple_MS_flt *Num_Files1grp A_1_Wp_2_T.img ... [[A_k_Wp_2_T.img]] R_1_Wp_2_T.img ... [[R_k_Wp_2_T.img]] SVT_MS_Pos.img SVT_MS_Neg.img*

Usually we refer to the first paradigm as A (activation) and the second one as R (rest). Let A.img and R.img be the two volumes we are analyzing and let T.img be our anatomical reference (template, "avgedit.img"). We denote by A_2_R.img the warped-and-resliced (using any algorithm) A.img in R.img space. There are at least 3 different ways one can transform A.img and R.img in T.img space, see “Techniques” section of this document.

where the following definitions are used:

Num_Files1grp
the number of volumes in one group (the two groups have an equal number of data sets

A_1_Wp_2_T.img
A(ctivation) paradigm data for subject 1, warped in T.img space

A_k_Wp_2_T.img
A(ctivation) paradigm data for subject **k**, warped in T.img space, 1<=**k**<=Num_Files1grp

R_1_Wp_2_T.img
R(est) paradigm data for subject 1, warped in T.img space

R_k_Wp_2_T.img
R(est) paradigm data for subject **k**, warped in T.img space, 1<=**k**<=Num_Files1grp

Prob_Atlas.img
The name of the file containing the probabilistic Atlas (lobes9_diff_intens.img)

SVT_MS_Pos.img and *SVT_MS_Neg.img*
The files where the (positive and negative) output of the multi-subject (MS) SVT statistical analysis will be saved

Examples:
SVT_simple_MS_flt Num_Files1grp ./A(1)Wp.img ... ./A(Num_Files1grp)Wp.img ./R(1)Wp.img ... ./R(Num_Files1grp)Wp.img ../lobes9_diff_intens.img ./A_R_SVT_MS_Pos.img ./A_R_SVT_MS_Neg.img

This command will use the post-processed groups of data (A's and R's are warped directly to the template, "avgedit.img") and the probabilistic partitioning information contained in "lobes9_diff_intens.img" to generate two multi-subject SVT output volumes (A_R_SVT_MS_Pos.img & A_R_SVT_MS_Neg.img) of the statistically significant differences between the two groups. Also look at the batch file "batch_SVT_MS". **Note** that the above example represents a **single** UNIX command-line.

- **Bootstrap_SVT**

Purpose:
This SVT command is used to statistically analyze the variations between groups of human brain functional volumes obtained under different stimulation paradigms.

You need to have all stereotactic data sets pre-processed according to the multi-subject part of the “Techniques” section of this document. The output SVT volumes are 4 byte (floating point) per pixel stereotactic images of size 181x217y181z. The first image contains the positive and the second contains the negatively statistically significant voxels. Intensities of both SVT output images are in the range [0, infinity] and represent the exact Z-scores. This procedure uses a BOOTSTRAP approach to correct the intensity threshold level for the large number of statistical tests across the 3D volume.

Usage:
bootstrap_SVT *1 Num_points Pt_1_X_coord Pt_1_Y_coord Pt_1_Z_coord Sigma_1 ... Pt_N_X_coord Pt_N_Y_coord Pt_N_Z_coord Sigma_N Num_Files1gr A_1_Wp_2_T.img ...*

[[A_k_Wp_2_T.img]] R_1_Wp_2_T.img ... [[R_k_Wp_2_T.img]] SVT_vol.img

Usually we refer to the first paradigm as A (activation) and the second one as R (rest). Let A.img and R.img be the two volumes we are analyzing and let T.img be our anatomical reference (template, "avgedit.img"). We denote by A_2_R.img the warped-and-resliced (using any algorithm) A.img in R.img space. There are at least 3 different ways one can transform A.img and R.img in T.img space, see “Techniques” section of this document.

where the following definitions are used:

1
just a flag!

Num_points (N)
the number of points we have manually identified, say on the SVT_simple volume, and we want to correct for multiple testing

Pt_i_X_coord
The X-coordinate (VOXEL coordinates, NOT world) for each 1 <= i <= N, selected point

Pt_i_Y_coord
The Y-coordinate for each 1 <= i <= N, selected point

Pt_i_Z_coord
The Z-coordinate for each 1 <= i <= N, selected point

Sigma_i
The estimate of the Regional standard deviation for each 1 <= i <= N. Obtained from the SVT_Simple-routine. These are the lobar stochastic estimates reported regionally by all SVT routines.

Num_Files1gr
The number of data files in each group (subtraction paradigm).

A_1_Wp_2_T.img
A(ctivation) paradigm data for subject 1, warped in T.img space

A_k_Wp_2_T.img
A(ctivation) paradigm data for subject **k**, warped in T.img space, 1<=**k**<=Num_Files1grp

R_1_Wp_2_T.img
R(est) paradigm data for subject 1, warped in T.img space

R_k_Wp_2_T.img
R(est) paradigm data for subject **k**, warped in T.img space, 1<=**k**<=Num_Files1grp

Prob_Atlas.img
The name of the file containing the probabilistic Atlas (lobes9_diff_intens.img)

SVT_vol.img
One of the SVT (floating point) volumes produced, say, by SVT_simple

Examples:
`SEE: bootstrap_SVT`

bootstrap_SVT 1 2 14 36 78 2.4 56 75 120 4.56 3 grp1_data1 grp1_data2 grp1_data3 grp2_data1 grp2_data2 grp2_data3 SVT_pos.img

This command will use the post-processed groups of data (A's and R's are warped directly to the template, "avgedit.img") and the probabilistic partitioning information contained in "lobes9_diff_intens.img" to generate two multi-subject SVT output volumes (A_R_SVT_MS_Pos.img & A_R_SVT_MS_Neg.img) of the statistically significant differences between the two groups. Also look at the batch file "batch_SVT_MS". **Note** that the above example represents a **single** UNIX command-line.

PRE- AND POST_PROCESSING PROCEDURES

- **flipMy3D_1**

Purpose:
This routine is used to flip the axes and/or invert the intensities of volumetric raw data. You will need to customize this code to fit your particular type of images. Remember, to recompile after each editing.

Usage:
flipMy3D_1 *xDim yDim zDim data_in.img data_Flipped_out.img*

where the following definitions are used:

xDim, *yDim* and *zDim*
Contain the dimensions of the volumetric data

data_in.img
Contains the name of the raw data file that needs a flip

data_Flipped_out.img
Contains the name of the raw data file that will contain the flipped image

Examples:
./flipMy3D_1 256 256 128 mri1.img mri1_FnI.img

This command will flip and invert (if needed) the image "mri1.img" of size 256x256y 128z, and

the result will be saved in the file "mri1_FnI.img" **Note** that the above example represents a **single** UNIX command-line.

- **histogram.out**

  Purpose:
  This code Creates the HISTOGRAM of a BINARY data set (1Byte or 4Byte data - data TYPE), and saves the histogram into a linear 1D binary (int) file

  Usage:
  See "batch_histogram"

  histogram.out

  where the following definitions are used:

  Activ_Data.img

  `Examples:`
  ./batch_histogram

- **get_MNI_ROI_info**

  Purpose:
  This program is used for determining the means and the variances of the overall and the 9 MNI probabilistic ROIs for groups of functional data. To get the average mean across all data and the average variance use this routine followed by "var.c" or batch_var. The continuously APPENDED file "Bin_output.img" will contain the 10 pairs of (mean, var), for every ROI, as floating point numbers (4 bytes), for each data set in the group.

  Usage:
  See "batch_MNI_ROI_info"

  get_MNI_ROI_info

  where the following definitions are used:

  Activ_Data.img

  `Examples:`
  ./batch_MNI_ROI_info

- **mean_var_bin1.out**

  Purpose:
  This code computes the MEAN and the VARINACE of a finite list of numbers Difference from

'mean_var_bin.c' is that it also writes out a binary array of 10 FLT point numbers containing the AVERAGED MEANS of each of the 10 ROI's across all subjects, this will be needed by 'interSubj_normROI1' and the SVT_Normalization GUI

Usage:
mean_var_bin1.out *Study_case_Bin Tot_Number_Vols* Bin_10ROI_means.img

where the following definitions are used:

Study_case_Bin
The input file, created and continuously appended by "batch_MNI_ROI_info", containing the means and variances for each subject's 9 MNI ROI's plus the global mean and variance.

Tot_Number_Vols
Total number of volumes in the study

Bin_10ROI_means.img
Binary file that will store the averaged ROI means across subjects - this will be needed by 'interSubj_normROI1'.

Examples:
./mean_var_bin1.out Study_case_Bin.img Tot_Number_Vols Bin_10ROI_means.img

This will use the binary data in "Study_case_Bin.img" to compute the across subject average (and it's variance) of the means of the 9 MNI ROI's. The resulting average means will be stored in "Bin_10ROI_means.img" and be available for the next step of the inter-subject normalization (interSubj_normROI1).

- **interSubj_normROI1**

Purpose:
This program is used to do INTER-SUBJECT normalization, based on the intensities of a selected "ROI" Example Making the mean of the CEREBELLUM equal to a fre-fixed number, like the average cerabellum-mean across subjects, and driving the rest of the data intensities along LINEARLY without altering the variance of the data - this is a simple linear shift, that brings the avg-ROI intensity to the desired level. The difference from 'interSubj_normROI' is that this routine reads a binary file, created by 'mean_var_bin1.out', which contains 10 FLT point values representing the AVERAGE means across subjects of the 10 MNI ROI's. Then depending on which Reference ROI is chosen by the user, using SVT_GUI_intensNorm, we select automatically the value of 'WhatMeanValue' by using the inputted 'Which_ROI'.

Usage:
See "batch_normalize_inter"

where the following definitions are used:

Activ_Data.img

Examples:
./batch_normalize_inter

- **intraSubj_normPutamen**

  Purpose:
  This program is used to do INTRA-SUBJECT normalization, based on the intensities in the "PUTAMEN". It allows equating either the mean only, or the first two moments of each of the probabilistically defined structures of interest to the first (two) moment(s) of the signal over the "putamen".

  Usage:
  intraSubj_normPutamen *Which_normalization Data_in.img prob_atlas.img Data_norm_out.img*

  where the following definitions are used:

  Which_normalization
  Which_normalization=1, for equalizing the means only, and Which_normalization=2 for equalizing the first two moments

  data_in.img
  The file containing the raw data whose intensities will be perturbed

  prob_atlas.img
  The file containing the probabilistic atlas (lobes9_diff_intens.img)

  Data_norm_out.img
  The output of the normalization (intrasubject rescaled data_in).

  Examples:
  ./intraSubj_normPutamen.out 1 pet1.img lobes9_diff_intens.img pet1_normlz_putamen.img

  This command will transform the intensity level of "pet1.img" so that the new 9 probabilistic structures of interest, defined in the atlas "lobes9_diff_intens.img", have the same mean as the mean of the putamen. **Note** that the above example represents a **single** UNIX command-line.

JAVA-BASED GRAPHICAL USER INTERFACE TO SVT

Currently we have implemented a JAVA based application that simplifies the usage of the SVT software. The Java_SVT_GUI is easy to install and very handy for running large scale brain data analyses or any number of volumes in a repetitive fashion.

1. change the working directory to SVT5_2.dir/SVT_Java.dir

2. Edit your "~/.cshrc" file by adding the following path-name: setenv CLASSPATH .:/fill_path_name/SVT5_2.dir/SVT_Java.dir:/fill_path_name/SVT5_2.dir/SVT_Java.dir/Java_1_FnI3D.dir:/fill_path_name/SVT5_2.dir/SVT_Java.dir/Java_2_makeaheader.dir:/fill_path_name/SVT5_2.dir/SVT_Java.dir/Java_3_warps.dir:/fill_path_name/SVT5_2.dir/SVT_Java.dir/Java_4_intensNorm.dir:/fill_path_name/SVT5_2.dir/SVT_Java.dir/Java_5_SVT.dir:/fill_path_name/SVT5_2.dir/SVT_Java.dir/Java_6_Viz.dir Remember to run source ~/.cshrc once you have edited the ".cshrc" file Where "fill_path_name" stands to the location where you have installed the SVT package
3. Installing SVT_GUI: type csh README inside /fill_path_name/SVT5_2.dir/SVT_Java.dir/
4. To Run SVT_GUI, go to the directory where your data is and type java Java_SVT_main

SUB-VOLUME THRESHOLDING (SVT) TECHNIQUES FOR ANALYZING FUNCTIONAL IMAGES

The following explains (step-by-step) the procedures one needs to follow to do the SVT (Sub-Volume Thresholding) statistical Analysis for determining the statistically significant regions of activation in (single or multiple studies of) Functional Data. This technique, has been proposed by: I. Dinov, P. Thompson, R. Woods, M. Mega, C. Holmes, DW Sumners, S. Saxena and A. Toga. The same group of researchers has done implementation, testing and documentation of this method.

I. SINGLE-SUBJECT STUDIES

These studies involve determining statistically significant metabolic changes of a single-subject scanned twice, under baseline (referred to as "Rest") and stimulus (referred to as "Act", for activation) conditions.

Suppose A.img and R.img are the two raw volumes of size X * Y * Z, where X is the fastest-varying index and Z is the slowest-varying index, it does not matter if the image represents transverse (axial), sagittal or coronal planes.

The following describes the exact order of the steps to get a correct final analysis:

1. computerName%> csh batch_myFnI3D
   This step is only necessary if the files need to be non-trivially Flipped, or intensities Inverted (FnI, Flip & Invert). Sometimes, if the raw images came from other formats (NIH) some of the x_step, y_step or the z_step can be negative (like -1), which means that the dimensions are reversed. You can use a properly selected line of "batch_raw2minc" to convert the raw data file "*.img" into a "*.mnc" (MINC-format) file that you can visualize (using: my_host%> Display file.mnc) to see if you'd need a flip.)

   Note: "jot" can be replaced by any other editor like "vi", "pico", "edit" etc. to properly edit batch and source files)

   - jot batch_raw2minc, with the proper voxel size, dimensions and volume orientation - sagittal, transverse, coronal;
   - Display file.mnc, to visually inspect for a need of an FnI, Flip & Invert;
   - jot batch_myFnI3D, edit properly the batch file, giving the file name of the volume to be flipped, dimensions etc;

- csh batch_myFnI3D, execute (do) the FnI;

  (For many volumes of the same type (protocol) this could be done simultaneously for all volumes in one pass).

2. computerName%> csh batch_makeaheader
   This makes the appropriate headers of the raw files. You'd need to know the volume dimensions and the voxel-size. These headers are in AIR format (Mayo Clinic, UK) and are needed by the AIR registration routines.)

   - jot batch_makeaheader, edit properly the file. All headers could be created in one pass only;
   - csh batch_makeaheader, after the correct editting is done, execute the batch_command_file.

3. computerName%> csh batch_warps
   This does two things: First it warps the A.img to R.img (registers A to R), call the new resliced volume A2R.img. Second, it warps A2R.img and R.img to "avgedit.img" – the reference "Average" anatomical MRI volume associated with the probabilistically defined search regions (In the MNI atlas - caudate, cerebellum, frontal, insula, occipital, parietal, putamen, temporal lobes, thalamus). Currently, "avgedit.img" contains the average_53_MNI study, which is the core of the currently used probabilistic atlas (ROI's).

   Call the new (resliced) volumes A2R2Avg.img and R2Avg.img (Note: This second step can vary a little depending on the study of interest - see "(3)" in Multi-Subject Analysis). Of course, both warping and reslicing are performed at each step separately.

   After this stage, the "A2R2Avg.img", "R2Avg.img", "avgedit.img" and "lobes9_diff_intens.img" should all look registered (convert them to *.mnc and visualize using " computerName %> register.opengl file1.mnc file2.mnc"). The file "lobes9_diff_intens.img" contains a mask data for the ROI's – probabilistically defined. 1 <= Caudate <=20 25<=Cerebellum <= 45, 50<=Frontal<=70, 75<=Insula<=95, 100<=Occipital<=120, 125<=Parietal<= 145, 150<=Putamen<=170, 175<=Temporal<195, 200<=Thalamus<=220. These are the corresponding intensities of the mask_file and of course, higher_intensities mean higher probabilities, lower_intensities mean lower probabilities - of the corresponding voxel being inside the ROI. All the warpings use Roger Woods AIR auto-image registration tool.

   - jot batch_warps, edit properly the batch file;
   - csh batch_warps, execute the batch.

Note: It may be wise to concatenate the field (.air & .warp) files and reslice only once, instead of reslicing twice, since interpolation done twice will degrade the results a little. See batch_warps_combine.

4. computerName%> csh batch_normalize
   This will do the inter-subject normalization. It equalizes the first two moments of the signals, mean & variance. Some studies also may require intra-subject normalization, where the intensities of each volume are normalized to those of the "putamen", see "intraSubj_normPutamen" and the

corresponding batch file. Typically the putamen and cerebellar intensities are more stable, and rarely show severe atrophies. That is why they can be used as references.

5. computerName%> csh batch_SVT
   This does the necessary Single-Subject stat_analysis on the difference image (A2R2Avg.img - R2Avg.img). Call the output A_R_SVT.img.

   - jot batch_SVT, edit properly the batch file;
   - csh batch_SVT, execute the batch.

Note: If you ever change the probabilistic ROI atlas you will need to execute: "varEstCorrRandFct1.out" and "extrSurBoxProbStr.out".

The first routine determines the necessary CF's (correction factors) for the variance estimates (required for the stat_analysis), based on the shape of the ROI's. The second one merely finds the smallest bounding box about each ROI and needs to be executed first (speeds up the computations), and its outputs need to be fed into all of the following routines. The outputs of "varEstCorrRandFct1.out" also need to be used in all routines that follow.

6. computerName%> csh batch_raw2minc1
   This final step converts the A_R_SVT.img to A_R_SVT.mnc (remember to look at both: the positively and negatively statistically significant SVT images).

   - jot batch_raw2minc1, edit correctly the batch file;
   - csh batch_raw2minc1, execute the batch.

7. computerName%> register.opengl ./avgedit.mnc ./A_R_SVT.mnc
   This shows in register the output of the stat_analysis. Visualize the SVT statistics on top of the anatomical "avgedit.mnc" or the functionl data or overlayed on the probabilistic atlas "lobes9_diff_intens.mnc".

II. MULTIPLE-SUBJECT STUDIES

These studies involve determining statistically significant metabolic changes for multiple subjects. They can be used for determining variations between groups (like amnestic and memory-retrieval-deficit groups) or for analyzing data for a single group of subjects each scanned twice, under baseline (referred to as "Rest") and stimulus (referred to as "Act", for activation) conditions (right versus left-handed subjects performing finger-opposition task, for example).

Suppose A(k).img and R(k).img are the Active (or group 1) raw volumes and Rest (or group 2) raw volumes ALL of size X * Y * Z, where X is the fastest-varying index and Z is the slowest-varying index, it does not matter if the image orientation is transverse (axial), sagittal or coronal.

The following describes the exact order of the steps to get a correct final analysis (this is very similar to part I.):

1. computerName%> csh batch_myFnI3D
   As in I. do flips if need be.

2. computerName%> csh batch_makeaheader
   As in I. make ALL headers.

3. computerName%> csh batch_warps
   Warp ALL to one of them, best representing the anatomy of the subjects being studied - as in I. This is the first registration step. Now there are at least three variations for the second warping step. Call the resliced volumes A(k)_2_A*.img, R(k)_2_A*.img, and the corresponding fields A(k)_2_A*.air, R(k)_2_A*.air, where "A*.img" is one of the data sets chosen as a reference volume.

   i. Warp the resulting resliced volumes to the average: "avgedit.img". Obtain the fields A(k)_2_A*_2_Avgedit.F, R(k)_2_A*_2_Avgedit.F, where "F" stands for "air" (for affine) or "warp" (for non-linear) polynomial registration fields. Reslice using these fields to get the final registered volumes.

   ii. As in (i) obtain the fields "A(k)_2_A*_2_Avgedit.F" and "R(k)_2_A*_2_Avgedit.F", but use "combine_air" or "combine_warp" (for combining linear followed by a non linear fields). Call the combined fileds "A(k)_Dbl_2_Avg.F" and "R(k)_Dbl_2_Avg.F". Finally, reslice using these new fileds.

   iii. Using the resliced volumes from warping step one find the "average" of the volumes: "A&R_Avgd_2_A*.img". Then register "A&R_Avgd_2_A*_2_Avgedit.img" to "avgedit.img", using an affine or non-affine warp, call the field "A&R_Avgd_2_A*_2_Avgedit.air/warp". To get the final registration of A1 to "avgedit.img" (going through A*.img) combine A1_2_A*.air followed by "A&R_Avgd_2_A*.img" and reslice using the combined field. Similarly for the other A(K) and the R(K) volumes.

   The bottom line is that the second field-to-be-applied is always the same: "A&R_Avgd_2_A*_2_Avgedit.air/warp" - it does not depend on A(k) or (R(k). A variation of (iii) is re-registering "A(k).img" ..., "R(k).img" to "A&R_Avgd_2_A*.img" obtaining new first fields: "A1_2_Avgd.air" etc. and then use these as the first fields into to "combine_air/warp" as in (3.2.3), instead of using "A1_2_A*.air".

4. computerName%> csh batch_normalize
   Normalization, as in I.

5. computerName%> csh batch_SVT_MS
   To do the Multi_subject_SVT stat_analysis

6. computerName%> csh batch_raw2minc1
   To make "*.mnc" file of the result

7. computerName%> register.opengl ./avgedit.mnc ./A_R_SVT_MultSubj.mnc
   To visualize the results of the statistical analysis, SVT technique.

NOTE: " computerName " can be replaced by the name of the SGI host you are logged on to.

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