

Optimally-Discriminative Voxel-Based Analysis

Software User Manual

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1. Introduction

This software package implements the Optimally-Discriminative Voxel-based Analysis (ODVBA) [1], which is used to determine the optimal spatially adaptive smoothing of images, followed by applying a voxel-based group analysis.

Voxel-based Analysis and Statistical Parametric Mapping (VBA-SPM) [2] of imaging data have offered the potential to analyze structural and functional data in great spatial detail, without the need to define a priori regions of interest (ROIs) and assumptions. Gaussian smoothing of images is an important step in VBA-SPM; it accounts for registration errors and integrates

imaging signals from a region around each voxel being analyzed. However, it has also become a limitation of VBA-SPM based methods, since it is often chosen empirically, non-optimally, and lacks spatial adaptivity to the shape and spatial extent of the region of interest.

ODVBA provides a mathematically rigorous framework for determining the optimal spatial smoothing of structural and functional images, prior to applying voxel-based group analysis. In order to determine the optimal smoothing kernel, a local discriminative analysis, restricted by appropriate non-negativity constraints, is applied to a spatial neighborhood around each voxel, aiming to find the direction best highlights the difference between two groups in that neighborhood. Since each voxel belongs to a large number of such neighborhoods, each centered on one of its neighboring voxels, the group difference at each voxel is determined by a composition of all these optimal smoothing directions. Permutation tests are used to obtain the statistical significance of the resulting Optimally-Discriminative VBM (ODVBA) maps.

The software package exploits some randomly selected data from the Alzheimer's Disease Neuroimaging Initiative (ADNI) [3] as an example to show the usage of the ODVBA.

2. Preprocessing Steps

2.1 Supported Image Formats

The software supports the ANALYZE 7.5 and NIFTI formats, where the voxel type of the scalar input images is either float (DT_FLOAT) or short (DT_SIGNED_SHORT).

2.2 Preparation of the Subjects List

For input convenience, one subjects list file in below format is used by all programs:

```
<Number of Patients M> <Number of Normal Controls N>
/base/path
<Path to image of patient 1>
.
.
.
<Path to image of patient M>
<Path to image of control subject 1>
.
.
.
<Path to image of control subject N>
```

On the first line, the number of patients is given followed by the number of control subjects, where these two numbers are separated by one or more whitespace characters. The second line specifies the base path to image files either absolute or relative to the directory in which the

subjects list file is located. The subsequent lines contain the paths to the image files, first the ones of the patients and second the ones of the control subjects. These paths can be given either relative, in which case they are considered relative to the base path specified on line two, or absolute. Note that the filename extensions `.nii`, `.hdr` or `.img` can be omitted.

A sample subject list file from data retrieved as part of the Alzheimer's Disease Neuroimaging Initiative (ADNI) is shown below. This sample file contains 100 subjects.

```
50 50
./images
003_S_1059-2006-11-09_RAVENS_GM_ds_le
011_S_0010-2005-11-07_RAVENS_GM_ds_le
011_S_0053-2005-11-14_RAVENS_GM_ds_le
.
.
.
003_S_0907-2006-09-11_RAVENS_GM_ds_le
011_S_0002-2005-08-26_RAVENS_GM_ds_le
011_S_0005-2005-09-02_RAVENS_GM_ds_le
.
.
.
```

2.3 Creating the Index File

The `odvba-index` command-line utility determines the indices of voxels in the set of input images whose average voxel value exceeds a certain threshold. Hence, it determines the indices of voxels relevant to the group analysis and outputs them to a text file which in turn is used as input to the command-line utility considered next and particularly the main program which performs the group analysis.

Example:

```
odvba-index ${ODVBA_EXAMPLE_DIR}/subjects.txt
```

2.4 Creating the Neighborhood Indices File

The `odvba-ni` command-line utility can be used to randomly selects a certain number of neighborhoods, specified by the `--ni-num` option of the program, from all neighborhoods in order to reduce the computational cost of the group analysis. The selected neighborhoods are used to form the learning sets on which the discriminative coefficients are calculated. Moreover, from each neighborhood a random number of samples, specified by the `--ni-voxels` option is drawn. The neighborhood information is stored in a file referred to as neighborhood indices file. This file can be re-used when performing the group analysis at different time points while ensuring that the same neighborhoods are considered. Note that the main program, when not

given a neighborhood file, will select the neighborhoods randomly. The size of each neighborhood has to be specified in physical units, i.e., millimeters, using the option `--ni-size`.

Example:

```
odvba-ni ${ODVBA_EXAMPLE_DIR}/subjects.txt \  
--ni-num 10000 --ni-voxels 400 --ni-size 15
```

3. Performing the group analysis

This command implements the core computation involved in the ODVBA method:

- 1) Local Non-negative Discriminative Projection
- 2) Determining each voxel's statistic
- 3) Permutation tests

You can generate the p-value map based on the input files which were created during the preprocessing steps using the command-line utilities `odvba-index` and `odvba-ni`.

Example:

```
odvba ${ODVBA_EXAMPLE_DIR}/subjects.txt --index index.txt --ni ni.txt \  
--perm-num 100 --phi 1
```

Alternatively, the creation of the index file and/or the neighborhood indices file can be omitted and the main program be called with the subjects list as input and the required arguments to sample the neighborhoods prior to the execution of the group analysis. Note that if you have a MPI library installed, you can use the command `odvba-mpi` to perform the group analysis on a cluster, utilizing more than one available slot.

Example:

```
mpiexec -np 10 odvba-mpi --ni-num 10000 --ni-voxels 400 --ni-size 15 \  
--perms-num 100 --phi 1 ${ODVBA_EXAMPLE_DIR}/subjects.txt
```

4. References

- [1] T. Zhang, C. Davatzikos, Optimally-Discriminative Voxel-Based Analysis, *Proceeding of International Conference on Medical Image Computing and Computer-Assisted Intervention*, vol. 13, no.2, pp: 257-265 (2010)
- [2] Ashburner, J., Friston, K.J.: Voxel-based morphometry-the methods. *Neuroimage*, 11(6) 805–821 (2000)
- [3] Alzheimer's Disease Neuroimaging Initiative: www.loni.ucla.edu/ADNI