MOE: Mixture-of-Experts Software Manual

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1 Introduction

This software can be used for datasets where the reference group ("controls") and the affected group ("patients") cannot be separated by a single line ("hyperplane"). MOE combines multiple hyperplanes along with a clustering objective, to split the affected group into multiple sub-groups. This is done in such a manner that each of the resulting sub-group is separable from the reference group by a single line.

See Figure 1, where the reference group is denoted by circles, and the affected group by triangles. In Case1, the affected group is not heterogeneous, as it is seperable from the reference group with a single line. Cases 2, 3, 4 require multiple lines to separate the affected group from the reference group.

This software works with data saved in comma-separated value format. Input features can be based on any type of data - volumes, density, connectivity, diffusion, clinical scores, cognitive data etc.

For more details, please read:
`Eavani, H., Hsieh, M. K., An, Y., Erus, G., Beason-Held, L., Resnick, S., Davatzikos, C. (2016). Capturing heterogeneous group differences using mixture-of-experts: Application to a study of aging. NeuroImage, 125, 498-514.`

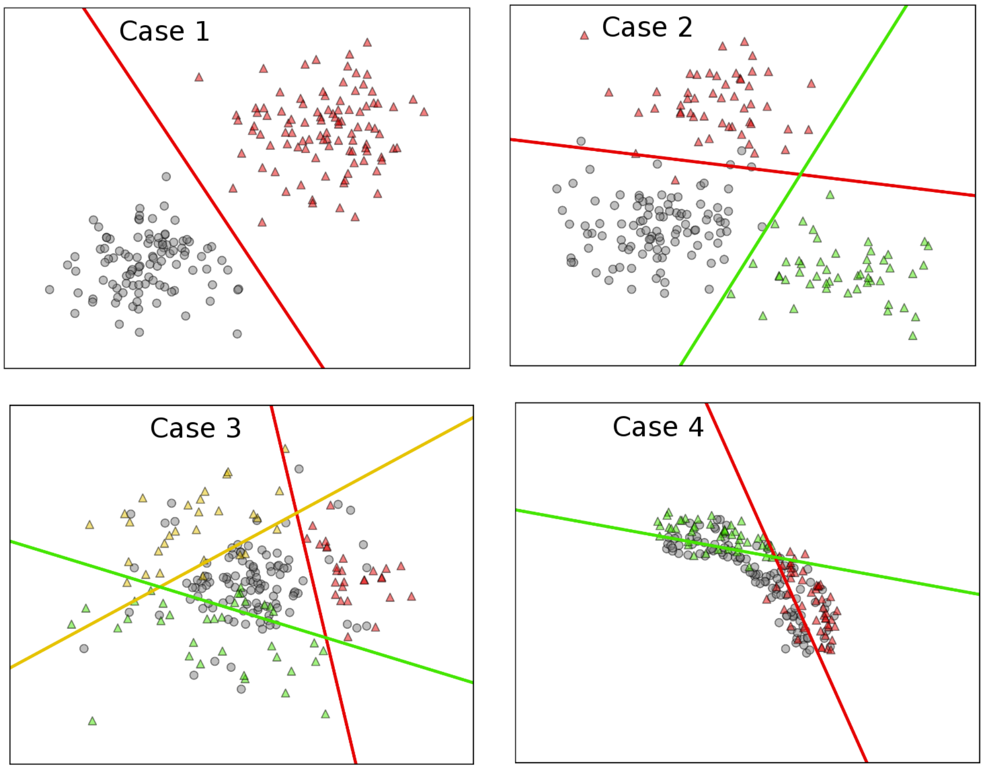


Figure 1: Four test cases with circles as the reference (controls) . Case 1 has no heterogeneity, as the reference and affected group (triangles) are separable by a single line. Case 2, 3, and 4 have different amounts of heteroegeity - MOE is able to find 2, 3 and 2 affected sub-groups respectively. These are indicated by different colors for the data points and associated hyperplanes.

2 Method

Consider a binary classification problem with data $\mathbf{x}_i \in \mathbf{R}^D$ obtained from $i = 1, 2, \dots N$ subjects. Each subject is associated with a binary label $y_i \in \{-1, 1\}$, -1 for the reference group and $+1$ for the affected group.
Let $\mathbf{m}_i = \left[m_i^1, m_i^2, \dots, m_i^K\right],\ m_i \in [0, 1], \sum_{k=1}^{K} m_i^k = 1$ indicate the relative membership of subject i to group k.
MOE is a joint model that combines ℓ_1-loss, ℓ_2-regularized SVM and a Fuzzy-C Mean clustering objective. The optimization problem is given below.

$$\underset{\{\mathbf{w}^k\}_k, \{m_i^k\}_{i,k}}{\text{minimize}} \quad \sum_{k=1}^{K} \left\{ \frac{1}{2} \left|\left|\mathbf{w}^k\right|\right|_2 + C \sum_{i=1}^{N} m_i^k \left(1 - y_i(\mathbf{w}^k)^T \mathbf{x}_i\right)_+ + t \sum_{i=1}^{N} (m_i^k)^a \left|\left|\mathbf{x}_i - \mathbf{d}^k\right|\right|_F^2 \right\}$$

subject to

$$\sum_{k=1}^{K} m_i^k = 1,\ m_i^k \in [0, 1] \quad n = 1, \dots, N \tag{1}$$

where t is a user-defined value that controls the trade-off between the cost of classification and clustering. The other user-defined parameters are the number of groups K, and the SVM cost-value C.
The "fuzzyness " coefficient m controls the "softness" of the membership assignments. In our model, we set the "fuzziness" coefficient a to a value of 2.
We use alternating minimization to solve for the cluster centroids $\mathbf{d}^k$, membership values m_i^k and the SVM hyperplanes $\mathbf{w}^k$. We use lib-svm with weighted samples to solve each of the $\mathbf{w}^k$, a quadratic-program to solve for m_i^k and the centroids have an analytical solution.
Given a new test case, its label y^* is determined as the sign of the weighted (based on its membership to each of the clusters) combination of individual SVM predictions.
Regression The regressed version uses Ridge regression in place of linear SVM. However please note that this extension of the code has not been extensively tested, nor published.

3 Software

3.1 Within main directory

1. Detailed documentation is contained in the latex file UserManual.tex and the pdf UserManual.pdf produced from it.

2. Author information is in AUTHORS.txt

3. All information needed to get started with the software is in README.md

4. The file INSTALL.txt has installation and usage information.

5. Doxyfile is the configuration file for generating doxygen documentation.

6. ignore.txt contains a list of files that doxygen ignores from parsing.

7. The folder docs/ will contain all the documentation once doxygen is run using Doxyfile.

8. The folder src/ contains source code for MOE.

9. The folder licenses/ contains license information related to this software.

3.2 Within `src/` directory

This software is implemeted entirely in Python.

1. Main python script is moe. This function parses input arguments, and calls SV_fuzzy to run the method. It also reads and saves output csv files. It calls RepeatedKFold if needed, if the -f argument is > 0.

2. RepeatedKFold.py Repeated evaluation of K fold cross-validation.

3. SV_fuzzy.py The main function that implements the method. It takes as input data matrices in numpy format, and returns output also in numpy format. It calls QP.py for solving membership values.

4. QP.py It sets up the quadratic program for solving membership values.

5. test.py This script runs all four test cases, and calls draw_moe_plot.py to plot results.

6. draw_moe_plot.py This script plots the output for the two-dimensional test cases.
7. MOEUtils.py Contains set of generic functions for checking file existence, exit status, etc.
8. The python script make copies all python files to correct places in the install directory.

4 Testing and Installation

4.1 Dependencies

This software has been primarily implemented for Linux operating systems.

- Python 2.7.9
- Python library numpy 1.7.2
- Python library scipy 0.15.1
- Python library pandas 0.16.2
- Python library sklearn 0.15
- Python library matplotlib 1.4.3

Make sure all dependencies are met before proceeding with install.

4.2 Testing

Run `./make test` from within the src directory.
This runs test.py on four test cases.
To test the software, we have provided synthetic two dimensional data for four test cases. In each of these cases, data points denoted by circles are the reference (control) samples, while points denoted by triangles are the affected (patient) cases which are made up of heterogeneous sub-groups. These are located in `src/test/Case*`. The image `test/All_test_results.png` shows the four test cases, it is also shown in Figure 1.
Test cases are used to check if the cross-validation accuracy in four test cases is greater than that of linear-SVM.
Proceed to the install step only if test passes in all four cases.

4.3 Installation

Run `./make install` from within the src directory, with the location of the install directory as the argument:

```
make install <installDir>
```

make creates four folders within installDir - bin, libexec, share and doc.

1. bin/ contains the main executible moe.
2. libexec/ has all python scripts.
3. share/ has the test data.
4. doc/ has the doxygen documentation.

Add the install directory to your path by running the following command. Replace `$installDir` with the location of the install directory from step 1 above.

```
export PATH=$PATH:$installDir/bin/
```

4.4 Code documentation

The "./make install" step (above) generates documentation in `$installDir/doc/*`.

5 Usage

```
moe --
Runs MOE-based heterogeneity classification on spreadsheet data
Works on any set of features -
Average regional volume/density/diffusion/connectivity,
clinical scores, cognitive data, etc

For best performance, pick optimal -c and -t values based on cross-validation

Usage: moe [OPTIONS]

Required Options:
[-d --data]         Specify the spreadsheet with list of ROIs
[-p --prefix]       Specify the prefix of the output file
```

```
[-H --header]       Specify the header column that has the discrete labels
[-l --label]        Specify the label for the heterogenous group

Options:
[-n --nSVMs]        Specify the number of SVMs as a number. Default = 2.
[-c --cost]         Specify the SVM cost value. Default = 1.
[-t --tradeoff]     Specify the classification vs. clustering tradeoff.
 Default = 0.1.
[-f --folds]        Specify the number of cross-validation folds to run.
 Default = 0. (not run)

[-o --outputDir]            The output directory to write the results.
  Defaults to the location of the input file
[-w --workingDir]           Specify a working directory.
 By default a tmp dir is created and used
[-u --usage | -h --help]    Display this message
[-v --verbose]              Verbose output
[-V --Version]              Display version information
```

To run this software you will need:

1. An input csv file, with the following mandatory fields:
   (a) Subject index in the first column
   (b) Header row containing feature names in the first row
   (c) A column containing the binary group labels - the name of the column and the value of the patient group (of whose heterogeneous sub-groups you want to find) needs to be provided in the command line options.

For a csv file `ROI_values.csv` that looks like below:

```
Subject_id, ROI_1, ROI_2, ROI_3, ..., Label, ...
BLSA_0001, 0.234, 0.4545, 0.212,...., AD , ...
BLSA_0002, 0.122, 0.1213, 0.3434,..., CN, ...
...
...
```

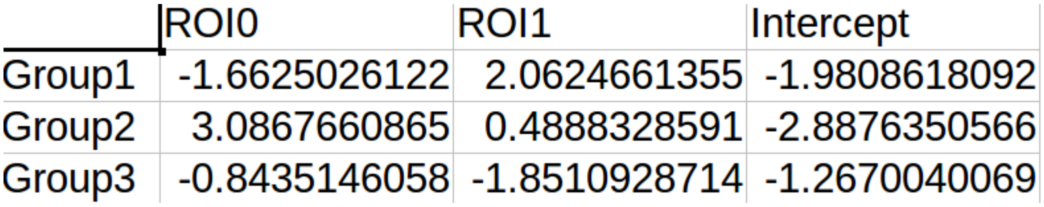
If you are looking for $N = 3$ sub-groups within the group with Label=AD, run the following command: Run the following command:

```
moe -d ROI_values.csv -p ROI_results -l AD -n 3 -o ./ -v
```

This will provide $N = 3$ hyperplanes and $N = 3$ sub-groups within the group with Label=AD.

In the output directory, the software returns:

1. One python numpy file containing all the results - `<prefix>_results_allResults.npz`
2. A csv file containing the hyperplanes, indexed against feature name in the first row. Filename `<prefix>_results_hyperplanes.csv`

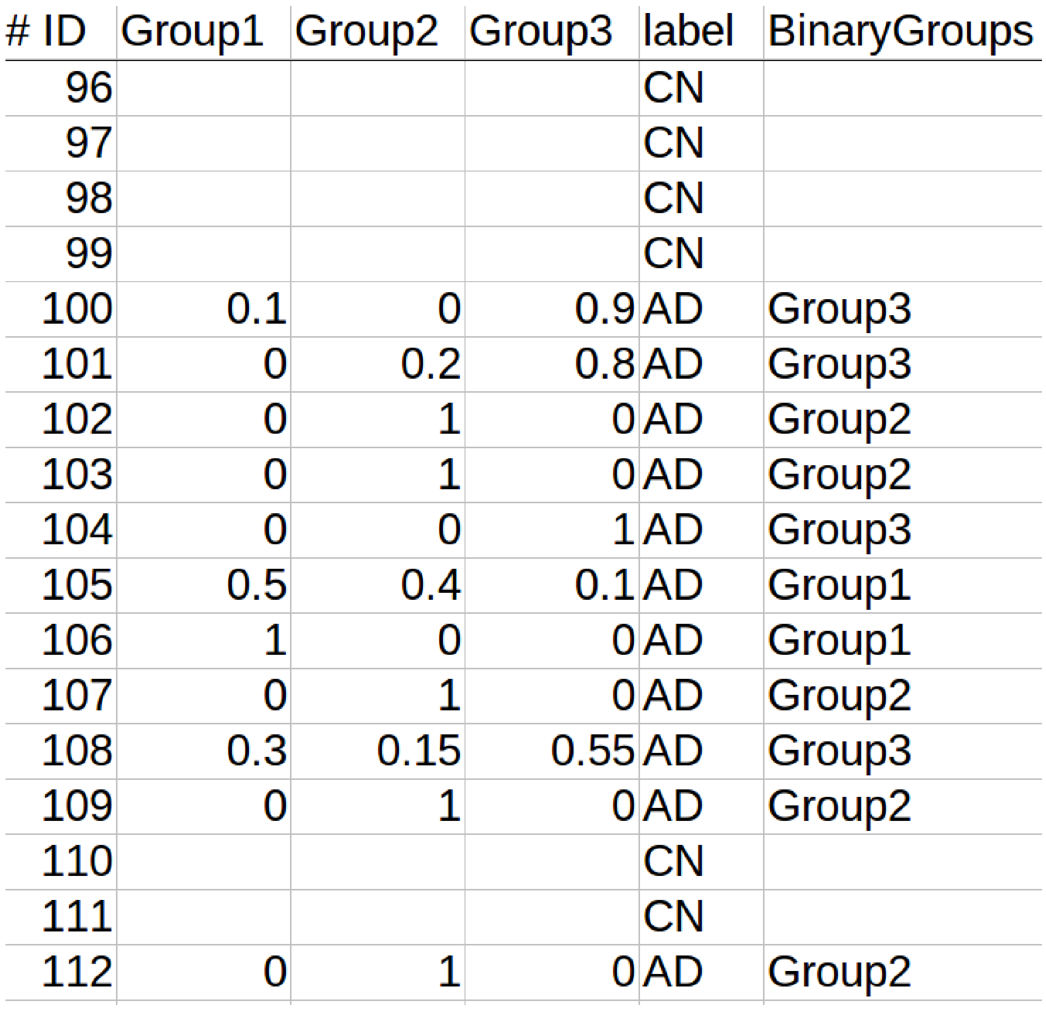


	ROI0	ROI1	Intercept
Group1	-1.6625026122	2.0624661355	-1.9808618092
Group2	3.0867660865	0.4888328591	-2.8876350566
Group3	-0.8435146058	-1.8510928714	-1.2670040069

Figure 2: A snapshot of a sample hyperplanes.csv file

   For example, Figure 2 shows a sample snapshot of the hyperplanes file. In this case, the value of each element of the hyperplane is indexed against ROI number (column) and group (rows). This value indicates the extent to which the ROI contributed to the classification of reference vs. that particular group.

3. A csv file containing the memberships, indexed against subject id in the first column. Filename `<prefix>_results_memberships.csv`



# ID	Group1	Group2	Group3	label	BinaryGroups
96				CN	
97				CN	
98				CN	
99				CN	
100	0.1	0	0.9	AD	Group3
101	0	0.2	0.8	AD	Group3
102	0	1	0	AD	Group2
103	0	1	0	AD	Group2
104	0	0	1	AD	Group3
105	0.5	0.4	0.1	AD	Group1
106	1	0	0	AD	Group1
107	0	1	0	AD	Group2
108	0.3	0.15	0.55	AD	Group3
109	0	1	0	AD	Group2
110				CN	
111				CN	
112	0	1	0	AD	Group2

Figure 3: A snapshot of a sample memberships.csv file

For example, Figure 3 shows a sample snapshot of the memberhsip file. This file has the membership value of each subject (row). The values under “Group 1”, “Group 2”, . . . denote soft memberships, and must sum to unity. The value under “BinaryGroups” reflects the maximum of the soft memberships. For example, for subject number 105, the membership values are 0.5, 0.4 and 0.1. As the maximum of these three values is Group1, this is saved under “BinaryGroups”. This value indicates the extent to which the ROI contributed to the classification of reference vs. that particular group.

4. A text file containing the accuracy of all “f” cross-validation folds, if it was specified. Filename `<prefix>_opt_cv.txt`

5.1 Choice of user-parameters

The user parameters n =number of sub-groups needs to be chosen using cross-validation. Choose the smallest value of n for which cross-validation accuracy is highest.

For example, for the data file ROI_values.csv (above), one may run ten fold cross-validation as follows (in bash script)

```
for n in {1..10}
do
  moe -d ROI_values.csv -p Res_${n}grps -l AD -n ${n} -f 10
done
```

and select the value of n for which the average value in `ROI_results_$ngroups_opt_cv.txt` is highest.

One can either use the default values for the other two user parameters: c = SVM cost and t = clustering-classfication trade-off. Else run grid-search as follows:

```
for c in 0.001 0.01 0.1 1 10 100 100
do
for t in 0.001 0.01 0.1 1 10 100 100
do
  moe -d ROI_values.csv -p Res_3grps_c${c}_t${t} -c ${c} -t ${t} \
                                                -l AD -n 3 -f 10
done
done
```

and select the value of c and t for which accuracy is highest, as before.

6 Citation

If you find this code useful, please cite:
Eavani, H., Hsieh, M. K., An, Y., Erus, G., Beason-Held, L., Resnick, S., Davatzikos, C. (2016). Capturing heterogeneous group differences using mixture-of-experts: Application to a study of aging. NeuroImage, 125, 498-514.