Package 'LESYMAP'

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Title Leions to Sympto	om Mapping in R	
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cognitive deficits of behavioral sco regression) and n available. LESYI	AP maps the specific brain areas responsible for by taking a series of lesion maps and a vector res. Both univariate (t-test, Brunner-Munzel, multivariate (sparse canonical corelations) tests are MAP is built to run both real and simulated m mapping analyses.	
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R topics docum	ented:	
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.createFolds

createFolds

Description

Used to create folds for k-fold validation

Usage

```
.createFolds(y, k = 10, list = TRUE, returnTrain = FALSE)
```

Arguments

```
y split sample by balancing y
```

k number of folds

list logical whether to return folds in a list

returnTrain logical whether to return training indices (T) or the test samples (F)

Author(s)

Caret Package

BM 3

ВМ

Massive Brunner-Munzel tests

Description

Takes a binary matrix of voxels and a vector of behavior and runs Brunner-Munzel tests on each voxel. This function is not compiled and is slow.

Usage

```
BM(lesmat, behavior)
```

Arguments

lesmat matrix of voxels
behavior vector of behavior

Value

Returned list with:

- statistic statistical values
- dof degrees of freedom

Author(s)

Dorian Pustina

Examples

```
set.seed(123)
lesmat = matrix(rbinom(200,1,0.5), ncol=2)
set.seed(123)
behavior = rnorm(100)
result = BM(lesmat, behavior)
```

BMfast

Fast Brunner-Munzel tests (v1)

Description

Takes a binary matrix of voxels and a vector of behavior and runs Brunner-Munzel tests on each voxel. This is a fast function, but may produce infinite values for perfectly separated group. Use BMfast2 which avoids this problem.

Usage

```
BMfast(X, y)
```

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Arguments

X binary matrix ov voxlels (columns) for all subjects (rows)

y vector of behavioral scores.

Value

List with two vectors: - statistic - BM values - dfbm - degrees of freedom

Author(s)

Dorian Pustina

/@export

BMfast2

Fast Brunner-Munzel tests (v2)

Description

Takes a binary matrix of voxels and a vector of behavior and runs Brunner-Munzel tests on each voxel. This is a fast function that corrects for infinite values with a similar approach as the nparcomp package.

Usage

```
BMfast2(X, y, computeDOF = TRUE)
```

Arguments

X binary matrix ov voxlels (columns) for all subjects (rows)

y vector of behavioral scores.

computeDOF (true) chooses whether to compute degrees of freedom. Set to false to save time

during permutations.

Value

List with two vectors:

- statistic BM values
- dfbm degrees of freedom

Author(s)

BMperm 5

Examples

```
set.seed(1234)
lesmat = matrix(rbinom(40,1,0.2), ncol=2)
set.seed(1234)
behavior = rnorm(20)
test = LESYMAP::BMfast2(lesmat, behavior)
test$statistic[,1] # -2.0571825 -0.8259754
test$dfbm[,1] # 16.927348 7.563432
```

 ${\tt BMperm}$

Fast Brunner-Munzel tests (v2) with permutations

Description

Takes a binary matrix of voxels and a vector of behavior and runs Brunner-Munzel tests on each voxel. This is a fast function that corrects for infinite values with a similar approach as the nparcomp package. It calculates p-values by running permutations of each voxel and using the ratio of times the real BM score exceeds the permuted BM score.

Usage

```
BMperm(X, y, computeDOF = TRUE, npermBM = 20000L, alternative = 1L)
```

Arguments

X	binary matrix ov voxlels (columns) for all subjects (rows)
У	vector of behavioral scores.
computeDOF	(default true) chooses whether to compute degrees of freedom. Set to false to save time during permutations.
npermBM	(default 20000) number of permutations to run at each voxel
alternative	(default 1) integer to select the tail of pvalues. 1-greater, 2-less, 3-two.sided

Value

List with these objects:

- statistic BM values
- dfbm degrees of freedom
- pvalue permutation-based probability value

Author(s)

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Examples

```
set.seed(1234)
lesmat = matrix(rbinom(40,1,0.2), ncol=2)
set.seed(1234)
behavior = rnorm(20)
test = LESYMAP::BMperm(lesmat, behavior, alternative=3)
test$statistic[,1] # -2.0571825 -0.8259754
test$dfbm[,1] # 16.927348  7.563432
test$pvalue[,1] # 0.1427929 0.4102795
```

checkAntsInput

checkAntsInput

Description

Function to check a variable whether is composed of an antsImage, list of antsImages, or simply filenames. If none of the above, an error is returned.

Usage

```
checkAntsInput(input, checkHeaders = F)
```

Arguments

```
input the variable to be checked checkHeaders make sure all images have the same headers
```

Value

Type of variable (antsImage, antsImageList, antsFiles) or error if variable cannot be established.

Author(s)

Dorian Pustina

Examples

```
## Not run:
    files = Sys.glob('/data/jag/nifti/*.nii.gz')
    myimagelist = imageFileNames2ImageList(files)
    checkAntsInput(myimagelist) # returns 'antsImageList'
    checkAntsInput(antsFiles) # returns 'antsFiles'
    checkAntsInput(myimagelist[[1]]) # returns 'antsImage'
## End(Not run)
```

checkFilenameHeaders 7

checkFilenameHeaders

checkFilenameHeaders

Description

Function to check that all filenames in a vector point to existing files with the same resolution, orientation, size, and origin.

Usage

```
checkFilenameHeaders(files, showError = T)
```

Arguments

files character vector of filenames

showError logical whether to show an error (True) or to return a boolean instead. Returned

values are True=pass,False=Fail

Value

logical if the test was successful or not

Author(s)

Dorian Pustina

checkImageList checkImageList

Description

Function to check that all antsImages in a list have the same orientation, origin, and resolution. The function stops with an error if one of the images has unusual headers. This behavior can be overcome by setting showError=F, and using the returned status (True=pass, False=fail) to make decisions outside this function.

Usage

```
checkImageList(imgList, showError = T, binaryCheck = F)
```

Arguments

imgList list of antsImages

showError boolean indicating whether to show the exact error and interrupt the function

(TRUE, default), or don't show the error and return the check status (FALSE).

The returned values when showError=F are T=passed or F=Failed.

binaryCheck boolean, check if images are binary (0/1 values). Useful when checking masks

or lesions. This check slows the output of the function.

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Value

True if list has images with same headers, otherwise False.

Author(s)

Dorian Pustina

Examples

```
## Not run:
files = Sys.glob('/data/jag/nifti/*.nii.gz')
myimagelist = imageFileNames2ImageList(files)
checkImageList(myimagelist) # no value returned
checkImageList(lesions, showError=F) # True returned
myimagelist[[4]] = cropIndices(myimagelist[[4]], c(1,1,1), c(20,20,20))
checkImageList(myimagelist) # error on image 4
## End(Not run)
```

checkMask

checkMask

Description

Function to check if mask is in the same space as inputs

Usage

```
checkMask(lesions.list, mask)
```

Arguments

```
lesions.list list of antsImages or character vector of filenames
mask antsImage of mask to check
```

Value

Nothing is returned, function stops with error if mask is not in the same space as images in lesions.list

Author(s)

getLesionLoad 9

getLesionLoad

Description

Computes lesion loads from a series of images. A parcellation image (or simple mask) is required to define the regions from which to compute the lesion load.

Usage

```
getLesionLoad(lesions.list, parcellation, label = NA, mask = NA,
binaryCheck = F, keepAllLabels = F, minSubjectPerLabel = "10%")
```

Arguments

```
lesions.list list of antsImages or filenames. Must be binary (0 and 1 values).
parcellation ansImage or filename of the parcellated volumes. A parcellation is an image
                  brain regions showned as with integer values (i.e. ,1,2,3,...).
label
                  (default=NA) you can ask to get output for a specific label in the parcellation
                  volume (i.e., label=122).
                  (default=NA) if this mask is specified (antsImage or filename) lesioned voxels
mask
                  outside the mask are ignored. This is not a good choice, but in case you need it
                  its there.
                  (default=FALSE) check whether lesion maps are binary (0/1). Will output an
binaryCheck
                  error if lesion files are not binary.
keepAllLabels
                  (default=FALSE) by default labels are removed if affected in just few subjects.
                  Setting this to TRUE will keep all labels.
minSubjectPerLabel
                  minimum number of subjects a parcel must be lesioned to keep and return it.
```

Value

• outputMatrix of lesion loads between 0 and 1. 1 means 100% lesioned. Each column is a single parcel and each row a single subject. Parcel numbers are placed as column names.

Author(s)

Dorian Pustina

Examples

```
lesydata = file.path(find.package('LESYMAP'),'extdata')
filenames = Sys.glob(file.path(lesydata, 'lesions', '*.nii.gz'))
lesions = imageFileNames2ImageList(filenames[1:10])
parcellation = antsImageRead(
file.path(lesydata,'template', 'Parcellation_403areas.nii.gz'))
lesload = getLesionLoad(lesions, parcellation)
```

getLesionSize

getLesionSize

Description

Compute lesion sizes from a list of antsImages.

Usage

```
getLesionSize(lesions.list, showInfo = TRUE)
```

Arguments

lesions.list List of antsImages or vector of filenames. It is assumed that images are binary (0/1).

showInfo logical show or not informations/warnings

Value

vector of lesion sizes in mm3

Author(s)

Dorian Pustina

```
getUniqueLesionPatches
```

Unique Lesion Patches

Description

Compute unique patches of voxels with the same pattern of lesions in all subjects. Useful to understand the number of patterns that will be analyzed in a lesion dataset. A patch is a group of voxels, not necessarily close to each other, which have the same identical lesion pattern.

Usage

```
getUniqueLesionPatches(lesions.list, mask = NA, returnPatchMatrix = F,
    thresholdPercent = 0.1, binaryCheck = F, showInfo = T)
```

Arguments

lesions.list list of antsImages (faster) or filenames (slower)

mask

(default=NA) a mask image to restrict the search for patches. Will be automatically calculated if not provided. Normally the mask restricts the search only to voxels lesioned in >10% of subejcts. To set this proportion use thresholdPercent.

returnPatchMatrix

(default=FALSE) logical, should the matrix of patches be returned. This is used in lesymap to run the analyses.

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```
thresholdPercent
```

```
(default=0.1) voxels with lesions in less than this proportion of subjects will not be considered. I.e., 0.1 = 10\%.
```

```
binaryCheck (default=FALSE) set this to TRUE to verify that maps are binary.
showInfo (default=TRUE) logical indicating whether to display information.
```

Value

List of objects named as follows:

- patchimg antsImage with every voxel assigned a patch number
- patchimg.samples antsImage mask of one representative voxel for each patch. Can be used to extract the patchmatrix.
- patchimg.size antsImage with the patch size at every voxel
- patchimg.mask antsImage of the mask used to extract patches. Can be used to put back results when combined with patchindx.
- patchindx vector of patch membership for each voxel. Can be used to put back results in an image.
- npatches number of unique patches in the image
- nvoxels total number of lesioned voxels in patchimg.mask
- patchvoxels vector of voxel count for each patch
- patchvolumes vector of volume size for each patch
- patchmatrix matrix of patches. This is used in lesymap to save time when running repetitive analyses.

Author(s)

Dorian Pustina

Examples

```
lesydata = file.path(find.package('LESYMAP'), 'extdata')
filenames = Sys.glob(file.path(lesydata, 'lesions', '*.nii.gz'))
patchinfo = getUniqueLesionPatches(filenames[1:10]) # slower
lesions = imageFileNames2ImageList(filenames[1:10])
patchinfo = getUniqueLesionPatches(lesions) # faster
```

```
lesyload_mricron lesyload_mricron
```

Description

Function to load data from a previous analysis in MRIcron/npm in a ready format for use in lesymap

Usage

```
lesyload_mricron(valfile, imageFolder = NA, returnFilenames = F,
 checkHeaders = T, showInfo = T)
```

Arguments

valfile

mricron filename with extention *.val. The function will search for images in the same folder where valfile is located, unless you specify imageFolder. If any of the files listed in the .val file are not found in the folder, an error will be displayed.

imageFolder

(default=NA) folder to look for the image files

returnFilenames

(default=FALSE) By default the function will load the images in memory to speed up things in lesymap. This may require too much RAM memory in some cases, and you may want to use filenames instead, which requires less memory but is slower in lesymap.

checkHeaders (default=TRUE) Headers will be checked to make sure all images have the same

dimension/origin/resolution, etc.

showInfo

(default=TRUE) show information upon successful load

Value

List with the following information lesions - list of antsImages or vector of filenames behavior vector of behavioral scores

Author(s)

Dorian Pustina

lesymap

Lesion to Symptom Mapping

Description

Lesymap uses univariate and multivariate methods to map functional regions of the brain that, when lesioned, cause specific cognitive deficits. All is required is a set of Nifti images with the lesion of each subject and the vector of behavioral scores. Lesions must be already registered in template space, use 'antsRegistration' or other ANTs tools to achieve this. Lesymap will check that lesions are in the same space before running. By default, voxels with identical lesion patterns are grouped together in unique patches, and analysis are run on patches. Patch-based mapping decreases the number of multiple comparisons and speeds up the analyses. Multivariate mapping is performed using an optimized version of sparse canonical correlations (SCCAN).

Usage

```
lesymap(lesions.list, behavior, mask = NA, patchinfo = NA,
 method = "BM", correctByLesSize = "none"
 multipleComparison = "fdr", pThreshold = 0.05, flipSign = F,
 minSubjectPerVoxel = "10%", nperm = 1000, saveDir = NA,
 binaryCheck = FALSE, noPatch = FALSE, showInfo = TRUE, ...)
```

Arguments

lesions.list list of antsImages, or a vector of filenames, or a single antsImage with 4 dimensions

behavior vector of behavioral scores or filename pointing to a file with a single column of

numbers.

mask (default=NA) binary image to select the area where analysis will be performed.

If not provided will be computed automatically by thresholding the average le-

sion map at minSubjectPerVoxel.

patchinfo (default=NA) an object obtained with getUniqueLesionPatches or from a previ-

ous analyses. Useful for repetitive analysis to save time and avoid the computa-

tion of patches each time.

what tests to run, one of 'BM' (default), 'BMfast', 'ttest', 'welch', 'regres', 'regresfast', 'regresPerm', 'sccan', 'sccanRaw'.

BM - Brunner-Munzel non parametric test, also called the Generalized Wilcoxon Test. The BM test is the same test used in the npm/Mricron software. See (see Rorden (2007)).

BMfast - ultrafast Brunner-Munzel with compiled code. BMfast can be combined with multipleComparison='FWERperm' to perform permutation based thresholding in a short time.

ttest - Regular single tailed t-test. Variances of groups are assumed to be equal. This is the test used in the voxbo software. Relies on t.test function in R. It is assumed that 0 voxels are healthy, i.e., higher behavioral scores. See the alternative parameter for inverted cases. (see Bates (2003)).

welch - t-test that assumes unequal variance between groups. Relies on t.test function in R.

regres - linear model between voxel values and behavior. Uses the lm function in R. This is equivalent to a t-test, but is useful when voxel values are continuous. To model the effect of covariates use the "regresfast" method

regressast - ultrafast linear regressions with compiled code. This method allows setting covariates. If covariates are specified the effect of each voxel will be estimated with the formula:

behavior ~ voxel + covar1 + covar2 + ...

This method allows multiple comparison correction with permutation based methods "FWERperm" and "clusterPerm". If these corrections are required and covariates are specified, the effect of each voxel is established with the Freedman-Lane method (see Winkler (2014)).

regresPerm - linear model between voxel values and behavior. The p-value of each individual voxel us established by permuting voxel values. The lmPerm package is used for this purpose. Note, these permutations do not correct for multiple comparisons, they only establish voxel-wise p-values.

chisq-chi-square test between voxel values and behavior. The method is used when behavioral scores are binary (i.e. presence of absence of deficit). Relies on the chisq.test R function. By default this method corrects individual voxel p-values with the Yates method (the same approach offered in the Voxbo software).

 ${\tt chisqPerm}$ - chi-square tests. P-values are established through permutation tests instead of regular statistics. Relies on the ${\tt chisq.test}$ R function.

sccan - sparse canonical correlations (NEW). Multivariate method that considers all voxels at once. By default, lesymap will run a lengthy procedure to

method

determine the optimal sparseness value (how extensive the results should be). You can set optimizeSparseness=FALSE if you want to skip this optimization. The search for optimal sparsness provides a cross-validated correlation measure that shows how well the sparseness value can predict new patients. If this predicive correlation is below significance (i.e., below pThreshold), the entire solution will be ignored and a NULL result will be returned. Lesymap returns normalized (0-1) voxel weights converted to positive; you can use rawStat=TRUE to retain the original voxel weights. Note that both lesion and behavior data are scale and centered before running SCCAN (hardcoded in lsm_sccan). You must apply the same scaling if you were to predict behavioral scores with the obtained voxel weights.

correctByLesSize

whether to correct for lesion size in the analysis. Options are "none", "voxel", "behavior":

- "none": (default) no correction
- "voxel": divide voxel values by 1/sqrt(lesionsize). This is the method used in Mirman (2015) and Zhang (2014). This correction works only with 'regres' methods. Two sample comparisons (t-tests and Brunner-Munzel) use binary voxels and will ignore this correction.
- "behavior": residualize behavioral scores by removing the effect of lesion size. This works on all methods, but is more agressive on results.

multipleComparison

(default='fdr') method to adjust p-values. Standard methods include "holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr". (see p.adjust)

Permutation methods include:

"FWERperm" (permutation based family-wise threshold) is enabled with methods 'BMfast' and 'regresfast'. In this case, many analysis are run with permuted behavioral scores, and the peak score is recorded each time (see Winkler 2014). The optimal threshold is established at 95th percentile of this distribution (or whatever pThreshold you choose). You can choose to use as reference another voxel lower in the ranks by specifying another 'v' value (i.e., lesymap(..., v=10) will record the 10th highest voxel).

"clusterPerm" (permutation based cluster correction) is enabled for 'regresfast'. It records the maximal cluster size from many random permutations of the behavior score and sets a cluster threshold based on that distribution. You must select pThreshold (voxel-wise, default=0.05) and clusterPermThreshold (cluster-wise, default 0.05) to achieve optimal with this method.

pThreshold

(default=0.05) threshold statistics at this p-value (after corrections or permutations)

flipSign

 $logical\ (default=FALSE),\ invert\ the\ sign\ in\ the\ statistics\ image.$

minSubjectPerVoxel

(default='10%') remove voxels/patches with lesions in less than X subjects. Value can be speficifed as percentage ('10%') or exact number of subjects (10).

nperm

(default=1000) number of permutations to run when necessary.

saveDir

(default=NA) save results in the specified folder.

binaryCheck

logical (default=FALSE), make sure the lesion matrix is 0/1.

noPatch

logical (default=FALSE), if True avoids using patch information and will analyze all voxels. It will take longer and results will be worse due to more multiple comparison corrections. This argument is ignored when performing SCCAN analyses.

showInfo logical (default=TRUE), display time-stamped info messages
... arguments that will be passed down to other functions (i.e., sparsness=0.045)

Details

Several other parameters can be specified to lesymap() which will be passed to other called fuctions. Here are some examples:

permuteNthreshold - (default=9) for Brunner-Munzel tests only. Voxels lesioned in less than this number of subjects will undergo permutation-based p-value estimation. Useful because the BM test is not valid when comparing groups with N < 9. Note, permuted BM tests currently require the package 'nparcomp'.

clusterPermThreshold - threshold used to find the optimal cluster size when using 'cluster-Perm' multiple comparison correction.

alternative - (default='greater') for two sample tests (ttests and BM). By default LESYMAP computes single tailed p-values assuming that non-lesioned 0 voxels have higher behavioral scores. You can specify the opposite relationship with alternative='less' or compute two tailed p-values with alternative='two.sided'.

covariates - (default=NA) enabled for method = 'regresfast'. This will allow to model the effect of each voxel in the context of other covariates, i.e., formula "behavior \sim voxel + covar1 + covar2 + ...".

I,.e., lesymap(lesions,behavior, method='regresfast', covariates=cbind(lesionsize, age)).

If you choose permutation based thresholding with covariates, lesymap will use the Freedman-Lane method for extracting the unique effect of each voxel (see Winkler 2014, Freedman 1983)

template - antsImage or filename used for plotting the results if a saving directory is specified (see saveDir)

v - (default=1) which voxel to record for permutation based thresholding. Normally the peak voxel is used (1), but other voxels can be recorded. See Mirman 2017 for this approach.

Value

The following objects are typically found in the returned list:

- stat.img statistical map
- rawStat.img (optional) raw SCCAN weights
- pval.img (optional) p-values map
- zmap.img (optional) zscore map
- mask.img mask used for the analyses
- average.img map of all lesions averaged. Map is produced only if no mask is defined.
- callinfo list of details of how you called lesymap
- printedOutput terminal output in a character variable
- perm.vector the values obtained from each permutation
- perm.clusterThreshold threshold computed for cluster thresholding
- perm.FWERthresh threshold computed for FWERperm thresholding
- patchinfo list of variables describing patch information:
 - patchimg antsImage with the patch number each voxels belongs to
 - patchimg.samples antsImage mask with a single voxel per patch
 - patchimg.size antsImage with the patch size at each voxel

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- patchimg.mask the mask within which the function will look for patches
- npatches number of unique patches in the image
- nvoxels total number of lesioned voxels in mask
- patchvoxels vector of voxel count for each patch
- patchvolumes vector of volume size for each patch
- patchmatrix the lesional matrix, ready for use in analyses. Matrix has size NxP (N=number of subjects, P=number of patches)

Author(s)

Dorian Pustina

Examples

```
lesydata = file.path(find.package('LESYMAP'),'extdata')
filenames = Sys.glob(file.path(lesydata, 'lesions', 'Subject*.nii.gz'))
behavior = Sys.glob(file.path(lesydata, 'behavior', 'behavior.txt'))
template = antsImageRead(
    Sys.glob(file.path(lesydata, 'template', 'ch2.nii.gz')))
lsm = lesymap(filenames, behavior, method = 'BMfast')
plot(template, lsm$stat.img, window.overlay = range(lsm$stat.img))

## Not run:
# Same analysis with SCCAN
lsm = lesymap(filenames, behavior, method = 'sccan',
sparseness=0.045, optimizeSparseness=FALSE)
plot(template, lsm$stat.img, window.overlay = range(lsm$stat.img))
save.lesymap(lsm, saveDir='/home/dp/Desktop/SCCANresults')

## End(Not run)
```

 lsm_BM

lsm_BM

Description

Lesion to symptom mapping performed on a prepared matrix. Brunner-Munzel tests are performed using each column of the matrix to split the behavioral scores in two groups.

Usage

```
lsm_BM(lesmat, behavior, permuteNthreshold = 9, nperm = 10000,
alternative = "greater", showInfo = TRUE, ...)
```

Arguments

lesmat binary matrix (0/1) of voxels (columns) and subjects (rows). behavior vector of behavioral scores.

normut aNthrochald

permuteNthreshold

(default=9) Voxels lesioned in less than this number will undergo permutation based thresholding. See Medina et al 2010.

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```
nperm Number of permutations to perform when needed.

alternative (default="greater") It is assumed that healthy voxels (0) have greater behavioral scores. If your data follow an inverted relationship choose "less" or "two.sided".

showInfo display info messagges when running the function.

other arguments received from lesymap.
```

Value

List of objects returned:

- statistic vector of statistical values
- pvalue vector of pvalues
- zscore vector of zscores

Author(s)

Dorian Pustina

Examples

```
{
set.seed(123)
lesmat = matrix(rbinom(200,1,0.5), ncol=2)
set.seed(123)
behavior = rnorm(100)
result = lsm_BM(lesmat, behavior)
}
```

lsm_BMfast

lsm_BMfast

Description

Lesion to symptom mapping performed on a prepared matrix. Brunner-Munzel tests are performed using each column of the matrix to split the behavioral scores in two groups. This function relies on a compiled version for fast processing.

Usage

```
lsm_BMfast(lesmat, behavior, permuteNthreshold = 9,
  alternative = "greater", statOnly = FALSE, nperm = 1000,
  npermBM = 20000, FWERperm = FALSE, v = 1, pThreshold = 0.05,
  permuteAllVoxelsBM = FALSE, showInfo = FALSE, ...)
```

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Arguments

lesmat binary matrix (0/1) of voxels (columns) and subjects (rows).

behavior vector of behavioral scores.

permuteNthreshold

(default=9) Voxels lesioned in fewer than 9 subjects may yield incorrect p-values with Brunner-Munzel tests, so they need to identify pvalues through individualized permutations. This parameter sets the threshold to find which voxels need

permutations. See Medina et al (2010).

alternative (default="greater") It is assumed that healthy voxels (0) have greater behavioral

scores. If your data follow an inverted relationship choose "less" or "two.sided".

statOnly logical (default=FALSE), skips some computations, mostly for internal use to

speed up some things.

nperm (default=1000) Number of permutations to perform on entire volumes when

needed for multiple comparisons corrections (i.e., in FWERperm).

npermBM (default=20000) Number of permutations to perform at every single voxel be-

low permuteNthrehsold. Note, this argument is different from nperm, which controls volume-based permutations to perform multiple comparison cor-

rections with FWERperm.

FWERperm logical (default=FALSE) whether to perform permutation based FWER thresh-

olding.

v (default=1) which voxel to record at each permutation with FWERperm. All

software use the peak voxel (v=1), but you can choose a voxel further down the list to relax the threshold (i.e., v=10 for 10 highest voxel) (see Mirman (2017)).

pThreshold (default=0.05) what threshold to use for FWER

permuteAllVoxelsBM

(default=FALSE) whether to force the permutation-based p-value calulation for all voxels, instead of applying only to voxels below permuteNthrehsold. Setting this option to TRUE will force all voxels undergo permutation-based

p-value calculation.

showInfo display info messagges when running the function.

... other arguments received from lesymap.

Value

List of objects returned:

- statistic vector of statistical values
- pvalue vector of pvalues
- zscore vector of zscores
- perm. vector (optional) vector of permuted statistics
- perm.FWERthresh (optional) permutation threshold established from the distribution of perm.vector

Author(s)

Dorian Pustina

Note on zscores quorm gives same values as MRIcron and relies on the normal distribution. however, we are computing t-scores, and should have relied on that distribution, which is the t-score itself. Ism_chisq 19

Examples

```
{
set.seed(123)
lesmat = matrix(rbinom(200,1,0.5), ncol=2)
set.seed(123)
behavior = rnorm(100)
result = lsm_BMfast(lesmat, behavior)
}
```

lsm_chisq

lsm_chisq

Description

Lesion to symptom mapping performed on a prepared matrix. The behavior must be a binary vector. Chi square tests are performed at each voxel. By default the Yates correction is performed, use correct=FALSE if you need to disable it. The behavior must be a binary vector. Exact p-values can be obtained with permutation based estimatins.

Usage

```
lsm_chisq(lesmat, behavior, YatesCorrect = TRUE, runPermutations = F,
nperm = 2000, showInfo = TRUE, ...)
```

Arguments

```
binary matrix (0/1) of voxels (columns) and subjects (rows).

behavior vector of behavioral scores (must be binary.

YatesCorrect (default=T) logical whether to use Yates correction.

runPermutations
logical (default=FALSE) whether to use permutation based p-value estimation.

nperm (default=2000) The number of permutations to run.

showInfo display info messagges when running the function.

other arguments received from lesymap.
```

Value

List of objects returned:

- statistic vector of statistical values
- pvalue vector of pvalues
- zscore vector of zscores

Author(s)

lsm_regres

Examples

```
{
set.seed(123)
lesmat = matrix(rbinom(200,1,0.5), ncol=2)
set.seed(1234)
behavior = rbinom(100,1,0.5)
result = lsm_chisq(lesmat, behavior)
}
```

lsm_regres

lsm_regres

Description

Lesion to symptom mapping performed on a prepared matrix. Regressions are performed between behavior and each column in the lesmat matrix.

Usage

```
lsm_regres(lesmat, behavior)
```

Arguments

lesmat matrix of voxels (columns) and subjects (raws).

behavior vector of behavioral scores.

Value

List of objects returned:

- statistic vector of statistical values
- pvalue vector of pvalues
- zscore vector of zscores

Author(s)

Dorian Pustina

Examples

```
{
set.seed(123)
lesmat = matrix(rbinom(200,1,0.5), ncol=2)
set.seed(123)
behavior = rnorm(100)
result = lsm_regres(lesmat, behavior)
}
```

lsm_regresfast 21

|--|--|

Description

Lesion to symptom mapping performed on a prepared matrix. Regressions are performed between behavior and each column of the lesmat matrix. Fast function based on compiled code.

Usage

```
lsm_regresfast(lesmat, behavior, covariates = NA, FWERperm = F,
nperm = 1000, v = 1, pThreshold = 0.05, clusterPerm = F,
mask = NA, voxindx = NA, samplemask = NA,
clusterPermThreshold = 0.05, showInfo = T, ...)
```

Arguments

lesmat	matrix of voxels (columns) and subjects (rows).
behavior	vector of behavioral scores.
covariates	(default=NA) vector of matrix of covariates.
FWERperm	logical (default=FALSE) whether to run permutation based FWER thresholding.
nperm	Number of permutations to perform when needed.
V	(default=1) what voxel to record for FWER thresholding.
pThreshold	(default=0.05) Voxel-wise threshold.
clusterPerm	logical (default=FALSE), whether to perform permutation based cluster thresholding.
mask	(default=NA) antsImage reference mask used for cluster computations.
voxindx	(default=NA) indices of voxels to put in mask
samplemask	(default=NA) antsImage used to extract voxels back in a matrix.
clusterPermT	hreshold
	(default=0.05) threshold for cluster selection after obtaining cluster size distrubution.
showInfo	display info messagges when running the function.
	other arguments received from lesymap.

Value

List of objects returned:

- statistic vector of statistical values
- pvalue vector of pvalues
- zscore vector of zscores
- perm. vector (optional) vector of permuted statistics
- perm.FWERthresh (optional) permutation threshold established from the distribution of perm.vector
- perm.clusterThreshold (optional) permutation threshold established from the distribution of perm.vector

lsm_regresPerm

Author(s)

Dorian Pustina

Examples

```
{
set.seed(123)
lesmat = matrix(rbinom(200,1,0.5), ncol=2)
set.seed(123)
behavior = rnorm(100)
result = lsm_regresfast(lesmat, behavior)
}
```

lsm_regresPerm

lsm_regresPerm

Description

Lesion to symptom mapping performed on a prepared matrix. Regressions are performed between behavior and each column in the lesmat matrix. This function relies on the lmPerm package to run. The number of permutations required to reach stable p-values is established automatically. For this reason, the user cannot specify a predefined number of permutations.

Usage

```
lsm_regresPerm(lesmat, behavior)
```

Arguments

lesmat matrix of voxels (columns) and subjects (rows).

behavior vector of behavioral scores.

Value

List with vectors of statistic, pvalue, and zscore.

Author(s)

lsm_sccan 23

1sm sccan

Sparse canonical correlations for symptom mapping.

Description

Multivariate SCCAN adapted for lesion to symptom mapping purposes. By default an optimization routine is used to find the best sparseness value. If you specify sparseness manually, it will be validated to find the cross-validated correlation that can be obtained with that sparseness. You can skip the entire optimization/validation by choosing optimizeSparseness=FALSE. To understand SCCAN arguments, see sparseDecom2.

Usage

```
lsm_sccan(lesmat, behavior, mask, rawStat = F, showInfo = T,
  optimizeSparseness = T, tstamp = "%H:%M:%S", pThreshold = 0.05,
  mycoption = 1, robust = 1, sparseness = 0.045,
  sparseness.behav = -0.99, nvecs = 1, cthresh = 150, its = 20,
  npermsSCCAN = 0, smooth = 0.4, maxBased = FALSE,
  directionalSCCAN = TRUE, ...)
```

Arguments

lesmat matrix of voxels (columns) and subjects (rows).

behavior vector of behavioral scores.

mask antsImage binary mask to put back voxels in image.

rawStat logical (default=FALSE) whether to skip converting all weights to positive, nor-

malizing 0-1, and removing weights < 0.1. If TRUE, the raw voxel weights will

be returned as returned by sparseDecom2.

showInfo logical (default=TRUE) display messages

optimizeSparseness

logical (default=TRUE) whether to run the sparseness optimization routine. If false, the default sparseness value will be used. If sparseness is manually defined this flag decides if cross validated correlations will be computed for the defined

sparseness.

tstamp timestamp format used in LESYMAP

pThreshold (default=0.05) If cross validated correlations show significance below this value

the results are considered null and an empty map is returned.

mycoption (default=1) SCCAN parameter, see sparseDecom2
robust (ddefault=1) SCCAN parameter, see sparseDecom2

sparseness (default=0.045) SCCAN parameter. Setting this manually is not recommended.

For more, see sparseDecom2.

sparseness.behav

(default=-0.99) the amount of sparseness used for behavior. Not to be changed

for standard analyses.

nvecs (default=1) SCCAN parameter. Normally only one eigenvector of weights is ob-

tained in LESYMAP. Multiple maps/eigenvectors can be retrieved for mapping

full deficit profiles in the future. For more, see sparseDecom2

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cthresh (default=150) SCCAN parameter, see sparseDecom2 its (default=20) SCCAN parameter, see sparseDecom2

npermsSCCAN (default=0) SCCAN permutations. In theory can be used to determine if the

cross-correlation between the two sides (behavior and lesions) is not random. However, LESYMAP uses k-fold validations, which are faster; this option has

not been tested. For more, see sparseDecom2.

smooth (default=0.4) SCCAN parameter. Determines the amount of smoothing of weights

in image space performed by sparseDecom2. The current default value is somewhat arbitrary, it was not determined through systematic simulations.

maxBased (default=FALSE) SCCAN parameter. Removes voxels with weights smaller

than 10% of the peak weight during internal SCCAN iterations. Although similar to what is done in LESYMAP with standard SCCAN results, this strategy follows a different route, and produces different weights. The overall final result is, however, quite similar. This method is faster then the standard SCCAN call in LESYMAP, but has not been tested thoroughly. Note that the optimal sparseness obtained with maxBased=TRUE is not optimal when switching to

maxBased=FALSE.

directionalSCCAN

(default=FALSE) If TRUE, the upper and lower bounds of sparseness search will be negative. A negative sparseness permits positive and negative voxel weights, thus finding the direction of the relationship with behavior.

... other arguments received from lesymap.

Value

List of objects returned:

- statistic vector of statistical values
- pvalue vector of pvalues
- sccan.eig2 SCCAN weight for behavior column(s).
- sccan.ccasummary SCCAN summary of projection correlations and pvalues (if permutations were used)
- optimalSparseness (optional) optimal value found for sparseness
- CVcorrelation.stat (optional) Correlation between true and predicted score with k-fold validation using the optimal sparseness value
- CVcorrelation.pval (optional) p-value of the above correlation

Author(s)

Dorian Pustina

Examples

```
{
## Not run:
  lesydata = file.path(find.package('LESYMAP'), 'extdata')
  filenames = Sys.glob(file.path(lesydata, 'lesions', '*.nii.gz'))
  behavior = Sys.glob(file.path(lesydata, 'behavior', 'behavior.txt'))
  behavior = read.table(behavior, header=FALSE)[,1]
  avg = antsAverageImages(filenames)
  mask = thresholdImage(avg, 0.1, Inf)
```

Ism_ttest 25

lsm_ttest

lsm_ttest

Description

Lesion to symptom mapping performed on a prepared matrix. T-tests are performed using each column of the matrix to split the behavioral scores in two groups. If var.equal=TRUE the Welch test is performed instead.

Usage

```
lsm_ttest(lesmat, behavior, var.equal = T, alternative = "greater",
...)
```

Arguments

behavior vector of behavioral scores.

var.equal logical (default=TRUE) should the variance between groups considered equal (t-test) or unequal (Welch test).

alternative (default='greater') Sets the expected relationship between voxel value and behavior. By default voxels with zero are not lesioned, and behavior is expected to be higher, thus alternative='greater'. If the relationship in your data is inverted, use alternative='less', and if you don't know your data, use alternative='two.sided'.

... other arguments received from lesymap.

Value

List of objects returned:

- statistic vector of statistical values
- pvalue vector of pvalues
- zscore vector of zscores

Author(s)

26 minSegDistance

Examples

```
{
set.seed(123)
lesmat = matrix(rbinom(200,1,0.5), ncol=2)
set.seed(123)
behavior = rnorm(100)
result = lsm_ttest(lesmat, behavior)
}
```

minSegDistance

minSegDistance

Description

This function computes the metric displacement between two binary masks

Usage

```
minSegDistance(manual, predict, get = "all", binarize = F, label = 1)
```

Arguments

manual segmentation of class antsImage, used as reference

predict other antsImage to compare to manual

get (default='all') one of 'mean', 'max', 'min', or 'all'

binarize logical (default=FALSE) whether to binarize the input images

label (default=1) integer or vector of labels to binarize I.e., label=c(2,4) means label

2 from manual, and 4 from predict will be compared.

Value

```
Scalar (for 'mean', 'max', 'min') or list (for 'all'). Note, results are in milimeters
```

Note

max = Hausdorff distance

Author(s)

```
optimize_SCCANsparseness
```

Optimization of SCCAN sparseness

Description

Function used to optimize SCCAN sparseness for lesion to symptom mapping.

Usage

```
optimize_SCCANsparseness(lesmat, behavior, mask, nFolds = 4,
   sparsenessPenalty = 0.03, lowerSparseness = -0.9,
   upperSparseness = 0.9, tol = 0.03, justValidate = FALSE,
   cvRepetitions = ifelse(length(behavior) <= 30, 6,
   ifelse(length(behavior) <= 40, 5, ifelse(length(behavior) <= 50, 4, 3))),
   showInfo = TRUE, directionalSCCAN = TRUE, mycoption = 1,
   robust = 1, sparseness = NA, nvecs = 1, cthresh = 150,
   its = 30, npermsSCCAN = 0, smooth = 0.4,
   sparseness.behav = -0.99, maxBased = FALSE, ...)</pre>
```

Arguments

nvecs

```
lesmat
                 lesion matrix
                 behavior vector
behavior
mask
                 antsImage mask
nFolds
                 how many folds to use
sparsenessPenalty
                 penalty term
lowerSparseness
                 minimum searched sparseness
upperSparseness
                 maximum searched sparseness
t.ol
                 tolerance value, see optimize () in R
justValidate just check the CV of provided sparseness
cvRepetitions
                 number of cross-validations at each sparseness value. Dynamically set depend-
                 ing on sample size: \leq30 to 6 reps, \leq40 to 5 reps, \leq50 to 4 reps, \geq50 to 3
                 reps.
showInfo
                 logical (default=TRUE) display messages
directionalSCCAN
                 (default=TRUE) switching to FALSE will switch sparseness range in the posi-
                 tive side, 0.005 to 0.9
                 standard SCCAN parameter
mycoption
robust
                 standard SCCAN parameter
                 standard SCCAN parameter
sparseness
```

standard SCCAN parameter

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```
cthresh standard SCCAN parameter

its standard SCCAN parameter

npermsSCCAN SCCAN permutations

smooth standard SCCAN parameter

sparseness.behav what sparsness to use for behavior

maxBased standard SCCAN parameter

... other arguments received from lesymap or lsm_sccan.
```

Value

List with:

```
minimum - best sparseness value
objective - minimum value of objective function
CVcorrelation - cross-validated correlation of optimal sparness
```

Author(s)

Dorian Pustina

the optimization function Will run SCCAN on each training fold, compute behavior prediction on the test fold, and finally return a cross validated correlation from entire sample end of optimfun

```
print.lesymap print.lesymap
```

Description

Funciton to display some meaningful summary when a lesymap output is called in command line.

Usage

```
## S3 method for class 'lesymap'
print(x, ...)
```

Arguments

x the output from a lesymap() call.... useless for compatibility with default print.

Author(s)

```
registerLesionToTemplate
```

registerLesionToTemplate

Description

Brings lesion maps in template space by registering the subject\'s anatomical to the template and applying the same transform to the lesion. To improve the registration the anatomical image is bias corrected and denoised. In addition, you can choose to skull-strip the image and run a more careful registration brain-on-brain so that the skull does not impact the registration in any way. Note, for technical reasons the registration is performed counterintuitively by moving the template on the subject, and not the subject on the template. For this reason, to bring the subject in template space we use the inverse transformation. Also note, at the moment ANTsR does not produce an inverse affine transformation explicitly, both forward and inverse affine transforms are identical. You can use ANTs to compute the inverse, or tell ANTsR if you need to invert an affine matrix applying the transformations (see whichtoinvert).

Usage

```
registerLesionToTemplate(subImg, subLesion, templateImg = NA,
  templateBrainMask = NA, templateRegMask = NA, skullStrip = T,
  typeofTransform = "SyNCC", outprefix = "", tstamp = "%H:%M:%S",
  showInfo = T, ...)
```

Arguments

subImg antsImage or character filename of the anatomical image of the subject. Typi-

cally this is a T1-weighted MRI image, on which you drew the lesion map.

subLesion antsImage or character filename of the lesion map. Typically you draw this manually or obtain it from automated lesion segmentation software. You can try

our LINDA toolbox for an automated alternative. Yet, manual drawing can be

performed quickly and is preferred.

templateImg antsImage or filename of the anatomical template image. This image should be

with skull included.

templateBrainMask

antsImage or filename of the template brain mask. This mask is needed for

skull-stripped registrations.

templateRegMask

antsImage or filename of the template mask that includes the skull but no face.

Useful for improving the skull stripping process.

skullStrip logical whether to remove the skull and perform brain-on-brain registration.

typeofTransform

an antsRegistration parameter that controls the quality of registration. The default is SyNCC, which probably is the most robust and takes long (1-2

hours maybe). For faster registration you can try SyN.

outprefix character of the prefix where to save the output. If this is set, most of images and

transformations will be saved at the specified path/prefix. The folder must exist or you will get an error. It is passed without modification to antsReqistration.

tstamp format of the timestamp when displaying info messages.

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```
showInfo logical whether to show info messages or be completely quiet. If you want also verbose registration messages, please set verbose=TRUE.other arguments to pass to antsRegistration
```

Value

List of objects returned:

- subImg subject\'s image in native space (after some preprocessing)
- subLesion subject\'s lesion map in native space
- subImgTemplate subject\'s image in template space
- subLesionTemplate subject\'s lesion in template space
- subRegMask registration mask in native space
- templateImg the template used to register the subject
- templateBrainMask the brain mask of the template image
- subLesionTemplate the template mask with skull and no face
- registration\$inverse_subject2template transformation matrices subject to template
- registration\$forward_template2subject transformation matrices template to subject

Author(s)

Dorian Pustina

Examples

regresfast

Fast linear regressions

Description

Takes a matrix of voxels and a vector of behavior and runs fast regressions for each voxel. Covariates can be defined (i.e. age) to find the effect of each voxel on behavior within the context of other predictive factors.

Usage

```
regresfast(X, y, covariates, hascovar = FALSE)
```

save.lesymap 31

Arguments

X matrix of voxlels (columns) for all subjects (rows).

y vector of behavioral scores.

covariates matrix with one or more columns. Must be of same length as behavior. This

variable should always be set, and the next argument can tell if covariates should

be used or not.

hascovar logical to tell whether covariates should be used.

Value

List with:

- statistic regression t-score
- n number of subjects
- kxfm degrees of freedom.

Author(s)

Dorian Pustina

Examples

```
set.seed(1234)
lesmat = matrix(rbinom(40,1,0.2), ncol=2)
set.seed(1234)
behavior = rnorm(20)
test = LESYMAP::regresfast(lesmat, behavior, as.matrix(behavior), hascovar=FALSE)
test$statistic[,1] # 0.6915683 1.1434760
test$kxmat # 2
```

save.lesymap

Save the output of lesymap.

Description

Function to save the output of lesymap.

Usage

```
save.lesymap(lsm, saveDir, infoFile = "Info.txt", template = NA,
   saveTemplate = F, savePatchImages = T, plot.alpha = 0.8,
   plot.axis = 3, plot.quality = 8, outputLogFile = "outputLog.txt",
   ...)
```

32 simulateBehavior

Arguments

lsm	object obtained with lesymap()
saveDir	folder to save to, will be created if it doesn't exist.
infoFile	(default='Info.txt') what should be the filename of the file with information.
template	(default=NA) an antsImage to overlay the results to. If the template is provided, results will be plotted and saved as image.
saveTemplate	(default=FALSE) should the template image also be saved? Useful when passing the results to a colleague.
savePatchImag	ges
	(default=TRUE) should the patch images be saved
plot.alpha	see plot.antsImage
plot.axis	see plot.antsImage
plot.quality	see plot.antsImage
	other arguments to use for plot().

Value

Nothing is returned. Files saved include resulting maps and a descriptive file with a lot of information about the lesymap run.

Author(s)

Dorian Pustina

```
simulateBehavior Simulation of behavior scores from lesion maps
```

Description

Function simulate behavioral scores based on the lesion load of specific brain areas. Used to run simulation studies.

Usage

```
simulateBehavior(lesions.list, parcellation, label = NA, mask = NA,
errorWeight = 0.5, binaryCheck = FALSE, exponent = 1)
```

Arguments

lesions.list	list of lesions (antsImages) or vector of filenames.
parcellation	mask or parcellation image. If a parcellation is passed, lesion load will be computed for each different label (value) in the image. Zero and non-affected labels are not returned by default. The parcellation input can be an antsImage or a character vector pointing to a file.
label	(default=NA) if a parcellation scheme id being used, you can select which labels to simulate behaviors for (i.e., $c(101,43)$ to simulate behavior for labels with value 101 and 43 only). If not set a simulation will be returned from each parcel.

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mask	mask to restrict the count of lesioned voxels. It is not recommended to use a mask, because lesions should affect behavior as they are, without the user restricting the lesions to masks defined in post-processing.
errorWeight	(default= 0.5) the amount of error to be added, i.e., 0.5 means half of the simulation will be error, the other half signal
binaryCheck	(default=FALSE) check to make sure all lesions are binary
exponent	power exponent to elevate behavior in order to increase non-linearity relationship with lesion load. 1 is default, and 3 is what Wang (2013) reported as lesion load relationship with behavior.

Value

List of objectas returned:

- behavload a matrix of simulated behavioral scores. Each column shows simulation for a single parcel. Column names indicate the label number in the parcellation file.
- lesload same as behavload, but indicates lesions loads of the simulated regions.
- lesbehavCorrelation vector of Pearson correlations between lesion load and simulated scores.
- LesvolBehavCorrelation vector of Pearson correlations between lesion size and simulated scores.

Author(s)

Dorian Pustina

Examples

```
{
## Not run:
  lesydata = file.path(find.package('LESYMAP'),'extdata')
  parcellation = antsImageRead(
   Sys.glob(file.path(lesydata, 'template', 'Parcellation_403areas.nii.gz')))
  filenames = Sys.glob(file.path(lesydata, 'lesions', '*.nii.gz'))
  lesions = imageFileNames2ImageList(filenames)
  simBehavior = simulateBehavior(lesions.list = lesions, parcellation =
  parcellation, label = c(101,43))

## End(Not run)
}
```

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