Package 'brainImageR'

April 15, 2019

Type Package

Title A Framework for visualizing gene set enrichment throughout neurodevelopment

Version 1.0.0

Author Sara Linker [aut, cre]

Maintainer Sara B Linker <sara.linker@gmail.com>

Description BrainImageR is a package that provides the user with information of where in the human brain their gene set corresponds to. This is provided both as a continuous variable and as a easily-interpretable image. BrainImageR has additional functionality of identifying approximately when in developmental time that a gene expression dataset corresponds to. Both the spatial gene set enrichment and the developmental time point prediction are assessed in comparison to the Allen Brain Atlas reference data.

License CC BY-SA 4.0

LazyData TRUE

biocViews Software, Transcription, GeneSetEnrichment, GeneExpression, GenePrediction

VignetteBuilder knitr

Depends R (>= 3.5)

Imports BiocGenerics, ExperimentHub, ggplot2, grDevices, grid, gridExtra, methods, randomForest, RColorBrewer, stats, testthat

Suggets BiocStyle, utils

RoxygenNote 6.0.1

Suggests knitr, rmarkdown

URL https://github.com/saralinker/brainImageR

BugReports https://github.com/saralinker/brainImageR/issues

git_url https://git.bioconductor.org/packages/brainImageR

git_branch RELEASE_3_8

git_last_commit d830d5c

git_last_commit_date 2018-10-30

Date/Publication 2019-04-15

R topics documented:

`available_areanames` *List of areas that are present in a plotted brain slice*

Description

provides all brain areas within a slice for a refset.

Usage

```
available_areanames(composite, slice = NULL)
```

Arguments

`composite`	Object from either SpatialEnrichment or CreateBrain
`slice`	Section of the brain to be queried

Value

all areas present in the brain section of interest

Examples

```
#brainImageR:::loadworkspace()
##Load in a gene set
data(vth)
##calculate spatial enrichment
#composite <- SpatialEnrichment(vth, reps = 20, refset = "developing")
#available_areanames(composite, slice = 5)
```

`BrainMap` *Internal- Overlaps regional enrichment into a single section*

Description

`BrainMap` Merges maps from reColor

Usage

```
BrainMap(dim, tissueExp, Abrev, Files, slice, refset = c("developing",
    "adult"))
```

Arguments

`dim`	numeric dimensions of the original image
`tissueExp`	counts of genes per tissue, from SpatialEnrichment.
`Abrev`	character of all regions in the given section
`Files`	character of tiff images for each region
`slice`	integer of current slice
`refset`	character of reference brain map

Value

returns a matrix weighted by the gene overlap

Examples

```
##Internal to brainImageR,called within CreateBrain
#brainImageR:::loadworkspace()
##First load in a gene set
data(vth)
##calculate the spatial enrichment
#composite <- SpatialEnrichment(vth, reps = 20, refset = "developing")
#tissueExp <- Boot(composite)

##Select the slice of interest
#slice <- 4
#Files <- .cache[["EH1434"]][[slice]]
#dim <- .cache[["EH1436"]][[slice]]

#Select the region of interest
#Abrev <- .cache[["EH1438"]]
```

```
#abrev <- "VZ"


# map <- BrainMap(dim = dim ,
# tissueExp = tissueExp,
#  Abrev = Abrev, Files = Files,
#  slice = slice,
# refset = "developing")
```

`brainrange` *brainrange*

Description

creates a sequence of numbers from first to last by the given interval

Usage

```
brainrange(first = 0, last = 1, by = 1)
```

Arguments

`first`	starting value number
`last`	ending value
`by`	amount to move by in sequence

Value

vector of numbers

Examples

```
brainrange(1,10,0.5)
```

`Comp-class` *Comp keeps track of Spatial Enrichment calculations and parameters*

Description

Comp tracks the parameters and calculations throughout spatial gene set enrichment.

Slots

genes character vector of query genes

tissueExp1 named numeric vector of query gene count in tissues

tissueExp2 named numeric vector of avg.

random.matrix matrix of overlap at random, size = boot replicates

refset character noting developing or adult reference
background gene count in tissues

composite composite image matrix

Examples

```
comp <- methods::new(Class="Comp",
genes = c("a","b"),
tissueExp1 = c(10,12),
tissueExp2 =  c(10,13),
composite = matrix(0,nrow=10,ncol=10),
random.matrix = data.frame(matrix(0,nrow=10,ncol=10)),
refset = "developing"
)
```

CreateBrain *Overlap spatial enrichment information and anatomical organization*

Description

CreateBrain convert spatial enrichment into anatomical coordinates.

Usage

```
CreateBrain(composite, boot, slice, pcut = 0.05)
```

Arguments

composite	Comp object returned from SpatialEnrichment
boot	result from testEnrich including significance estimates
slice	integer brain section
pcut	numeric padj filter.

Value

Comp object

Examples

```
#brainImageR:::loadworkspace()
##First put together a gene list, or load in the default vth dataset
data(vth)
##Calculate the spatial enrichment.
#composite <- SpatialEnrichment(vth, reps = 20, refset = "developing")
#tissueExp1 <- composite@tissueExp1
#random.matrix <- composite@random.matrix
##Calculate the significance estimates
#boot <- testEnrich(composite)
##Color the brain section of interest with enrichment
#composite <- CreateBrain(composite, boot, slice = 6, pcut = 0.05)
##Plot the brain
#PlotBrain(composite, Breaks = 12)
```

---

dat *In vitro temporal data of human neural progenitor cells and neurons*

Description

RNA-seq data: Induced pluripotent stem cells were differentiated into neural progenitor cells (NPC.1, NPC.2, NPC.3, NPC.4) that were patterned for the forebrain lineage. Neurons were differentiated from these neural progenitor cells (Neurons.5, Neurons.6). RNA was collected from both NPCs and neurons, poly(A) cDNA libraries were generated, and sequenced on an Illumina HiSeq 2500. RNA-seq data was aligned to the human Hg19 reference, and counts were normalized into log2(TPM + 1) values. Gene names are in human symbol format.

Usage

```
dat
```

Format

10193 X 6 data.frame

GetGenes *GenGenes*

Description

`GetGenes` returns the genes that are expressed within a given tissue

Usage

```
GetGenes(genes, composite, tissue_abrev = NULL)
```

Arguments

`genes`	Query gene list.
`composite`	Result from SpatialEnrichment
`tissue_abrev`	The tissue of interest.

Value

Gene overlap between query and tissue of interest

Examples

```
#brainImageR:::loadworkspace()
##First put together a gene list, or load in the default vth dataset
data(vth)
##Calculate the spatial enrichment.
#composite <- SpatialEnrichment(vth, reps = 20, refset = "developing")
##Ask which genes are present in any given tissue.
#available_areanames(composite, slice = 4)
#vth_in_VZ <- GetGenes(vth, composite, tissue_abrev = "VZ")
```

---

hipp *Hippocampal genes using the adult human brain as reference*

Description

Hippocampal genes were identified using the differential search tool on the Allen Brain Atlas Human brain map. The hippocampal formation was contrasted to neighboring regions to identify a gene list that was enriched within the hippocampus.

Usage

```
hipp
```

Format

a vector with 1302 gene names

InABA *Quick search for presence of genes in the ABA list*

Description

InABA checks for the gene name in the ABA dataset

Usage

```
InABA(genes, refset = c("developing", "adult"))
```

Arguments

genes	genes to search
refset	reference brain map. developing (default) or adult

Value

returns the list of genes that are also present in the ABA dataset

Examples

```
#brainImageR:::loadworkspace()
##First load in a gene set
data(vth)
##Then query the dataset to see which genes are present
#vth_in <- InABA(vth)
#head(vth_in)
#length(vth_in) / length(vth)
```

PlotBrain *Color and Plot the SGSE image*

Description

PlotBrain Plots CreateBrain. The gene set enrichment observe within the microdissected tissues (results of testEnrich) are combined here to show gene set enrichment across broad brain regions. Enriched regions are colored in red, and regions depleted for the query gene list are colored in blue.

Usage

```
PlotBrain(composite, legend = TRUE)
```

Arguments

composite	Comp object returned from CreateBrain.
legend	Boolean whether the legend should be included. Default = TRUE

Details

PlotBrain plots your spatial gene set enrichment image.

Value

plots the SGSE brain image

Examples

```
##First put together a gene list, or load in the default vth dataset
#brainImageR:::loadworkspace()
data(vth)
##Calculate the spatial enrichment.
#composite <- SpatialEnrichment(vth, reps = 20, refset = "developing")
##Calculate the significance of the gene set enrichment
#boot <- testEnrich(composite)
##Color the brain section of interest
#composite <- CreateBrain(composite, boot, slice = 5, pcut = 0.05)
##Plot the brain
#PlotBrain(composite)
```

PlotEnrich *PlotEnrich*

Description

A quick plot to assess the enrichments returned from testEnrich. Gene overlap calculated by random chance is plotted on the x-axis and the gene overlap from the query set on the y-axis. Each dot represents an individual microdissected tissue. Note that the signficance estimate is only dependent on the randomly generated overlaps if the p-values were calculated with the bootstrap procedure.

Usage

```
PlotEnrich(boot)
```

Arguments

boot	Comp object returned from the testEnrich function

Value

Spatial enrichment plot

Examples

```
#brainImageR:::loadworkspace()
##First put together a gene list, or load in the default vth dataset
data(vth)
##Calculate the spatial enrichment
#composite <- SpatialEnrichment(vth, 20, "developing")
#tissueExp1 <- composite@tissueExp1
#random.matrix <- composite@random.matrix
##Calculate the significance estimates
#boot <- testEnrich(composite)
#PlotEnrich(boot)
```

PlotPred *Plot your temporal predictions*

Description

PlotPred Plots the temporal predictions.

Usage

```
PlotPred(time)
```

Arguments

time	Object returned from predict_time

Value

prediction plot

Examples

```
#brainImageR:::loadworkspace()
##Load in data
data(dat)
##predict time
#time <- predict_time(dat)
##plot the predictions
#PlotPred(time)
```

`Pred-class` *Pred*

Description

keeps track of parameters and results from predict_time

Slots

`pred_age` data.frame of results from predict_time

`model` randomForest model

`minage` minimum age filter from predict_time

`maxage` maximum age filter from predict_time

`tissue` tissue filter from predict_time

Examples

```
prep <- methods::new(Class="Pred",
pred_age = data.frame(matrix(0,nrow=10,ncol=10)),
model =  list(c(rep("A",5), rep("B",5))),
minage = 8,
maxage = 2120,
tissue = "HIP"
)
```

`predict_time` *Predict developmental time from gene expression data*

Description

Predict human developmental time from expression dataset

Usage

```
predict_time(dat = NULL, genelist = NULL, minage = 8, maxage = 2120,
    tissue = NULL, minrsq = 0.6)
```

Arguments

dat	Normalized expression matrix
genelist	Optional: restrict analysis to gene list
minage	min pcw of the reference set. default = 8
maxage	max pcw of the reference set. default = 2120
tissue	Optional: restrict analysis to tissue (available)
minrsq	(range 0-1) model leniency. default = 0.5.

Value

spatiotemporal predictions.

Examples

```
#brainImageR:::loadworkspace()
##Load in the data
data(dat)
##predict time
#time <- predict_time(dat)
```

PValue.onetail *Calculate p-value from bootstrapped sample*

Description

The distribution of microdissected tissues supporting each larger brain region is not equal across all regions. We therefore provide an option to bootstrap gene set enrichment. This function calculates the signficance of that enrichment.

PValue.onetail Calculates the p-value from a bootstrapped sample

Usage

```
PValue.onetail(regions, tissueExp1, random.matrix)
```

Arguments

regions	character regions to search
tissueExp1	numeric vector presence of genes in query
random.matrix	numeric presence of genes at random

Value

p-value of the significance of tissueExp1 given the random.matrix

Examples

```
##Internal to brainImageR, called within testEnrich
#brainImageR:::loadworkspace()
##First put together a gene list, or load in the default vth dataset
data(vth)
##Calculate the spatial enrichment.
#composite <- SpatialEnrichment(vth, reps = 20, refset = "developing")
#tissueExp1 <- composite@tissueExp1
#random.matrix <- composite@random.matrix
#boot <- PValue.onetail(regions = names(tissueExp1),
#tissueExp1,
#random.matrix)
```

RandomTissueSummary *Generate a random overlap*

Description

random overlap for background correction and bootstrapping

Usage

```
RandomTissueSummary(i, genes, samplesize, refset = c("developing", "adult"))
```

Arguments

i	current iteration
genes	all genes to sample from
samplesize	sample size to select from gene list
refset	reference map. developing (default) or adult

Value

returns a list of the random gene overlap for each tissue

Examples

```
##Internal to brainImageR, called within SpatialEnrichment
#brainImageR:::loadworkspace()
##First load in a gene set
data(vth)
#tissueExp <- RandomTissueSummary(1, vth, 20)
```

reColor *Color in the brain images based on enrichment values*

Description

reColor quantifies the presence of a gene list within each tissue

Usage

```
reColor(i, slice, tissueExp, dim, Abrev, Files, refset = c("developing",
    "adult"))
```

Arguments

i	tissue region from within the specified rostral-caudal section
slice	current slice
tissueExp	tissueExp1 from SpatialEnrichment.
dim	Original dimensions of the image
Abrev	list of tissue regions
Files	list of tiff images
refset	reference map. developing (default) or adult

Value

returns genes counts for each tissue

Examples

```
#brainImageR:::loadworkspace()
##First load a gene set
data(vth)
##calculate spatial enrichment
#composite <- SpatialEnrichment(vth,20,"developing")
#boot <- Boot(composite)
#subboot <- c(boot[boot$pvalue < 0.05 & is.finite(boot$FC), "FC"])
#names(subboot) <- rownames(boot[boot$pvalue < 0.05 & is.finite(boot$FC), ])
#tissueExp <- subboot
##Select the slice of interest
#slice <- 4
#Files <- .cache[["EH1434"]][[slice]]
#dim <- .cache[["EH1436"]][[slice]]
##Select the region of interest
#Abrev <- .cache[["EH1438"]][[4]]
#abrev <- "VZ"
#tmp <- reColor(abrev, slice, tissueExp, dim, Abrev, Files)
```

SpatialEnrichment *Calculate the presence of your gene set within each brain region*

Description

Calculates the presence of gene set within each region

Usage

```
SpatialEnrichment(genes, background = NULL, reps = 10,
    refset = c("developing", "adult"))
```

Arguments

genes	query gene set
background	background gene list, default = NULL (uses all ABA genes)
reps	replicates for bootstrap, default = 10
refset	reference brain map. developing (default) or adult

Value

"Comp" object

Examples

```
#brainImageR:::loadworkspace()
##First load in a gene set
data(vth)
##Then calculate the spatial enrichment
#composite <- SpatialEnrichment(vth,20,"developing")
```

testEnrich *Calculate significance of gene set enrichment*

Description

testEnrich test the enrichment of the observed enrichment

Usage

```
testEnrich(composite, method = c("fisher", "bootstrap"))
```

Arguments

composite	Comp object returned from SpatialEnrichment.
method	character either "bootstrap" or "fisher"

Value

spatiotemporal prediction

Examples

```
#brainImageR:::loadworkspace()
##First put together a gene list, or load in the default vth dataset
data(vth)
##Calculate the spatial enrichment.
#composite <- SpatialEnrichment(vth, reps = 20, refset = "developing")
##Calculate the significance estimates
#boot <- testEnrich(composite)
#boot <- boot[order(boot$FC, decreasing=TRUE),]
#head(boot)
```

`TissueSummary` *Internal-Identify the number of genes expressed in each tissue*

Description

. Quantifies the presence of gene list within each tissue

Usage

```
TissueSummary(genes, refset = c("developing", "adult"))
```

Arguments

`genes`	Genes to query for tissue location
`refset`	reference map. developing (default) or adult

Value

returns genes counts for each tissue

Examples

```
#Internal to brainImageR, used within SpatialEnrichment
#First load in a gene set
#brainImageR:::loadworkspace()
data(vth)
#tissueExp <- TissueSummary(vth, refset = "developing")
```

tis_in_region *List of regions that are supported by given tissue*

Description

Brain areas supported by tissue of interest. Opposite=tis_set()

Usage

```
tis_in_region(composite, tissue_abrev)
```

Arguments

composite	object returned from SpatialEnrichment or CreateBrain
tissue_abrev	abreviation of the microdissected tissue of interest.

Value

general brain areas

Examples

```
#brainImageR:::loadworkspace()
##Load in a gene set
data(vth)
##calculate spatial enrichment
#composite <- SpatialEnrichment(vth, reps = 20, refset = "developing")
#tis_in_region(composite, "LHAa")
```

tis_set *List of tissues that support a given region in the brain plot*

Description

Tissues that support brain area. Opposite=tis_in_region()‘

Usage

```
tis_set(composite, area.name, slice)
```

Arguments

composite	object returned from SpatialEnrichment or CreateBrain
area.name	abreviation of the brain area of interest.
slice	section of the brain to query (1-10)

Value

all areas supported by the tissue

Examples

```
#brainImageR:::loadworkspace()
##Load in a gene set
data(vth)
##calculate spatial enrichment
#composite <- SpatialEnrichment(vth, reps = 20, refset = "developing")
#get the set of tissues that are present within a given region
#tis_set(composite, area.name = "Pu", slice = 6)
```

---

vth *VTH genes identified from Allen Brain Atlas developing human*

Description

Ventral thalamus genes were identified using the differential search tool on the Allen Brain Atlas brain span (prenatal brain). The ventral thalamus was contrasted to neighboring regions to identify a gene list that was enriched within the vth.

Usage

```
vth
```

Format

A vector with 1389 gene names

---

whichtissues *Identify the tissues where a set of genes are expressed*

Description

Identifies which tissues express genes

Usage

```
whichtissues(g, refset = c("developing", "adult"))
```

Arguments

g	gene list
refset	reference map. developing (default) or adult

Value

Tissue regions

Examples

```
#brainImageR:::loadworkspace()
genes <- c("HOXB9", "HOXB10", "VIM")
#whichtissues(genes, refset = "developing")
```

Index