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Description This package contains functions to calculate the Specificity Index statistic, which can be used for comparative quantitative analysis to identify genes enriched in specific cell populations across a large number of profiles, as well as perform numerous post-processing operations. NOTE: Supplementary data (human & mouse expression sets, calculated pSI datasets, etc.) can be found in pSI.data package located at the following URL: http://genetics.wustl.edu/jdlab/psi_package/
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pSI-package

Specificity Index Statistic

Description

This package contains functions to calculate the Specificity Index statistic, which can be used for comparative quantitative analysis to identify genes enriched in specific cell populations across a large number of profiles, as well as perform numerous post-processing operations.

NOTE: Supplementary data (human & mouse expression sets, calculated pSI datasets, etc.) can be found in pSI.data package located at the following URL: http://genetics.wustl.edu/jdlab/psi_package/

Details

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Author(s)

Xiaoxiao Xu, Alan B. Wells, David OBrien, Arye Nehorai, Joseph D. Dougherty

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References


Candidate Gene Lists

This list contains 5 candidate gene lists. They are provided as sample gene lists to be used with fisher.iteration & candidate.overlap functions found in this package.

- candidate.genes$AutDB
  Autism spectrum disorder candidate gene list from AutDB (N=328)
candidate.genes

- candidate.genes$protein.disrupting.rdnv
  Autism spectrum disorder candidate gene list collected from 4 studies published in 2012 (N = 122)
- candidate.genes$silent.rdnv
  Autism spectrum disorder negative control gene list collected from 4 studies published in 2012 (N = 122)
- candidate.genes$hcrt.genes
  Narcolepsy Candidate Gene List (N=63)
- candidate.genes$retinopathy.genes
  Human Congenital Retinopathies Disease Gene List (N=120)

NOTE: Supplementary data (human & mouse expression sets, calculated pSI datasets, etc.) can be found in pSI.data package located at the following URL: http://genetics.wustl.edu/tdlab/psi_package/

Format

5 candidate gene lists, each in the form of a character vector, which are contained within one R list.

Details

- candidate.genes$AutDB
  Hand-curated list of Autism Spectrum Disorder (ASD) candidate genes derived from human genetics studies downloaded from AutDB (N=328)
- candidate.genes$protein.disrupting.rdnv
  List of Protein-Disrupting rare de novo variant affected genes in ASD Probands (N = 122)
- candidate.genes$silent.rdnv
  List of Silent rare de novo variant affected genes in ASD unaffected siblings (N = 122)
- candidate.genes$hcrt.genes
  List of differentially dysregulated genes from narcoleptic mice with Hcrt neuron ablation versus control (N=63)
- candidate.genes$retinopathy.genes
  List of genes identified in human congenital retinopathies downloaded from the curated RetNet database (N=120)

Source

AutDB

protein.disrupting.rdnv & silent.rdnv


Retinopathy genes
Daiger, SP. RetNet, the Retinal Information Network. https://sph.uth.edu/RetNet/

Examples

data(candidate.genes)
names(candidate.genes)
candidate.genes[[5]]

candidate.overlap Candidate Gene Overlap

Description
candidate.overlap Extracts genes specific to samples which overlap with a candidate gene list at various pSI thresholds

Usage

candidate.overlap(pSIs, candidate.genes, write.csv = FALSE)

Arguments

pSIs data frame output from specificity.index function with the number of columns equal to the number of samples and genes as rows.
candidate.genes candidate gene list tested for overrepresentation in cell types/samples. Comprised of official gene symbols.
write.csv logical variable indicating if csv files will be written to the current working directory (default value is FALSE)
Details

Returns list consisting of 6 data frames, one for each pSI threshold. Each data frame contains genes specific to each sample which overlap with a candidate gene list and whose pSI values fall below each respective threshold for each cell type/sample included in the analysis. NOTE: Supplementary data (human & mouse expression sets, calculated pSI datasets, etc.) can be found in pSI.data package located at the following URL: http://genetics.wustl.edu/jdlab/psi_package/

Author(s)

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Examples

```r
#Load sample pSI output
data(sample.data)
#Load sample candidate gene lists
data(candidate.genes)
#Generates lists of overlapping genes
candidate.gene.overlap.AutDB <- candidate.overlap(pSIs=sample.data$pSI.output,
                                                  candidate.genes=candidate.genes$AutDB)
```

Description

Differentially expressed genes (up-regulated & down-regulated) in cortices of autistic vs control subjects from human transcriptomic data. NOTE: Supplementary data (human & mouse expression sets, calculated pSI datasets, etc.) can be found in pSI.data package located at the following URL: http://genetics.wustl.edu/jdlab/psi_package/

Format

List containing two character vectors

Details

dataset.s1 is a list which contains two character vectors of differentially expressed genes. Differential expression was assessed using the SAM package (Significance Analysis of Microarrays), for FDR <.05 and fold change >1.3.

- `dataset.s1$up.regulated`
  - Up-regulated genes (N=234)
- `dataset.s1$down.regulated`
  - Down-regulated genes (N=229)
Source


Examples

data(dataset.s1)

---

**fisher.iteration**  
*Fisher’s Exact Test Across All Cell Types & pSI Thresholds*

**Description**

`fisher.iteration` will test a candidate gene list for overrepresentation in the various cell type/pSI threshold combinations produced by the `specificity.index` function. NOTE: Supplementary data (human & mouse expression sets, calculated pSI datasets, etc.) can be found in `psi.data` package located at the following URL: [http://genetics.wustl.edu/jdlab/psi_package/](http://genetics.wustl.edu/jdlab/psi_package/)

**Usage**

```r
fisher.iteration(pSIs, candidate.genes, background = "data.set", p.adjust = TRUE)
```

**Arguments**

- `pSIs`  
  data frame output from `specificity.index` function with the number of columns equal to the number of samples and genes as rows.

- `candidate.genes`  
  candidate gene list tested for overrepresentation in cell types/samples. Comprised of official gene symbols.

- `background`  
  character string used to indicate what background gene list should be used in Fisher’s exact test for overrepresentation. The default value is "data.set" which indicates that the gene list of the input pSI data set will be used to represent the background gene list. This would be used in the case when the input pSI data set is comprised of genes derived from the same species as the genes found in the candidate gene list. background can take on two other values, the first of which is "human.mouse". "human.mouse" indicates that the background gene list will be comprised of intersection of two lists: 1) all genes in the input pSI dataset (all are human genes), 2) all genes with clear human-mouse homologs. This option would be used in the case when the input data set is comprised of human genes (i.e. genes from a human microarray) and the candidate gene list being tested is comprised of mouse genes. The last value `background` can take on is "mouse.human". "mouse.human" indicates that the background gene list will be comprised of intersection of two lists: 1) all genes in the input pSI dataset (all are mouse genes), 2) all genes with clear mouse-human homologs. This option would be used in the case when the input data set is comprised of mouse genes (i.e. genes from a mouse microarray) and the candidate gene list being tested is comprised of human genes.
pSI.count

p.adjust logical. default output is bonferroni corrected p-value but if p.adjust is FALSE, nominal p-values will be output.

Details

This function is used to answer the question of what is the probability that a certain number of genes specific to a certain cell type/sample occurred by chance (as usual with low probabilities corresponding to high statistical significance). This is accomplished with a binary variable for each gene in the population with two mutual exclusive values: 1) The gene is specific to the cell type/sample in question or 2) The gene is not specific to the cell type/sample in question

Author(s)

Xiaoxiao Xu, Alan B. Wells, David OBrien, Arye Nehorai, Joseph D. Dougherty

Examples

##load sample pSI output
data(sample.data)
##load sample candidate gene lists
data(candidate.genes)
##run Fisher’s exact test for overrepresentation on pSI.out for the AutDB
##candidate gene list across all cell types/sample types & pSI thresholds
fisher.out.AutDB <- fisher.iteration(pSIs=sample.data$pSI.output,
  candidate.genes=candidate.genes$AutDB)

pSI.count

Convert pSI output to gene count list

Description

pSI.count This functions counts number of genes specific to each sample type

Usage

pSI.count(pSIs, write.csv = FALSE)

Arguments

pSIs data frame output from specificity.index function with the number of columns equal to the number of samples and genes as rows.
write.csv logical variable indicating if csv files will be written to the current working directory (default value is FALSE)
Details

Returns data frame consisting of 6 rows, one for each pSI threshold, and as many columns as cell types/samples were included in the analysis. Each cell type/sample will have a count of many genes whose pSI values fall below each respective threshold for each cell type/sample. NOTE: Supplementary data (human & mouse expression sets, calculated pSI datasets, etc.) can be found in pSI.data package located at the following URL: http://genetics.wustl.edu/jdlab/psi_package/

Author(s)

Xiaoxiao Xu, Alan B. Wells, David OBrien, Arye Nehorai, Joseph D. Dougherty

Examples

```r
# load sample pSI output
data(sample.data)
# Count the number of genes specific to each cell type/sample type across all pSI thresholds
psi.out.count <- psi.count(pSIs=sample.data$pSI.output, write.csv=TRUE)
```

---

`pSI.list`  
Convert pSI output to gene list

Description

`pSI.list` returns list consisting of 6 data frames, one for each pSI threshold.

Usage

```r
pSI.list(pSIs, write.csv = TRUE)
```

Arguments

- `pSIs`  
  data frame output from `specificity.index` function with the number of columns equal to the number of samples and genes as rows.

- `write.csv`  
  logical variable indicating if csv files will be written to the current working directory (default value is FALSE)

Details

Each data frame contains genes whose pSI values fall below each respective threshold for each cell type/sample included in the analysis. NOTE: Supplementary data (human & mouse expression sets, calculated pSI datasets, etc.) can be found in pSI.data package located at the following URL: http://genetics.wustl.edu/jdlab/psi_package/

Author(s)

Xiaoxiao Xu, Alan B. Wells, David OBrien, Arye Nehorai, Joseph D. Dougherty
Examples

```r
# load sample pSI output
data(sample.data)
# List the genes specific to each cell type/sample type across all pSI thresholds
psi.out.list <- psi.list(pSIs=sample.data$pSI.output, write.csv=FALSE)
```

---

**Sample Input & Output pSI Data Sets**

**Description**

Sample expression matrix and sample specificity index statistic (pSI) output data sets used to illustrate the pSI package functions. NOTE: Supplementary data (human & mouse expression sets, calculated pSI datasets, etc.) can be found in pSI.data package located at the following URL: http://genetics.wustl.edu/jdlab/psi_package/

**Format**

List comprised of two data frames.

**Details**

Sample expression matrix is the Brainspan RNAseq data condensed into 6 major regional divisions for just the young adult regions. Sample pSI output data set is calculated from the young adulthood Brainspan RNAseq data just previously described.

**Source**

http://www.brainspan.org

**Examples**

```r
data(sample.data)
```

---

**Specificity Index Statistic**

**Description**

`specificity.index` Calculates specificity index statistic (pSI) values of input expression matrix which can be used for comparative quantitative analysis to identify genes enriched in specific cell populations across a large number of profiles. This measure correctly predicts in situ hybridization patterns for many cell types. `specificity.index` returns a data frame of equal size as input data frame, with pSI values replacing the expression values. NOTE: Supplementary data (human & mouse expression sets, calculated pSI datasets, etc.) can be found in pSI.data package located at the following URL: http://genetics.wustl.edu/jdlab/psi_package/
Usage

specificity.index(pSI.in, pSI.in.filter, bts = 50, p_max = 0.1, e_min = 0.3, hist = FALSE, SI = FALSE)

Arguments

pSI.in data frame with expression values for genes in rows, and samples or cell types in columns (at this point replicate arrays have been averaged, so one column per cell type)

pSI.in.filter matched array (same genes and samples) but with NA’s for any genes that should be excluded for a particular cell type.

bts numeric. number of distributions to average for permutation testing

p_max numeric. maximum pvalue to be calculated

e_min numeric. minimum expression value for a gene to be included. For microarray studies, a value of 50 has been the default value and for RNAseq studies, a value of 0.3 has been used as the default.

hist logical. option for producing histograms of actual & permuted distributions of gene rank

SI logical. option to output SI value instead of default pSI value

Details

\[ SI_{n,1} = \frac{\sum_{k=2}^{m} \text{rank} \left( \frac{P_{k,n}}{P_{k,n}} \right)}{m-1} \]

Author(s)

Xiaoxiao Xu, Alan B. Wells, David OBrien, Arye Nehorai, Joseph D. Dougherty

References


Examples

# load sample expression matrix
data(sample.data)
# calculate specificity index on expression matrix
#(Normally for RNAseq data, and e_min of 0.3, microarrays: e_min= 50)
psI.output <- specificity.index(pSI.in=sample.data$pSI.input, e_min=20)
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